RADIOLOGICAL AND HISTOLOGICAL CORRELATION OF ULTRASOUND GUIDED FINE NEEDLE ASPIRATION OF FOCAL LIVER LESIONS

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CERTIFICATE

This is to certify that this dissertation entitled **"RADIOLOGICAL AND HISTOLOGICAL CORRELATION OF ULTRASOUND GUIDED FINE NEEDLE ASPIRATION OF FOCAL LIVER LESIONS"** is a bonafide work done by **Dr.CHITRAKALA SUGUMAR** , in partial fulfillment of the requirements of The TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY, Chennai for the award of M.D. Pathology Degree.

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I declare that this dissertation entitled **"RADIOLOGICAL AND HISTOLOGICAL CORRELATION OF ULTRASOUND GUIDED FINE NEEDLE ASPIRATION OF FOCAL LIVER LESIONS "** has been done by me under the guidance and supervision of **Prof.Dr.P.KARKUZHALI, M.D.,** It is submitted in partial fulfillment of the requirements for the award of the M.D., Pathology degree by The Tamilnadu Dr. M.G.R. Medical University, Chennai. This has not been submitted by me for the award of any degree or diploma from any other University.

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CONTENTS

INTRODUCTION

Fine needle aspiration (FNA) has proven to be a very effective means of obtaining tissue from many different body sites for diagnosis. Fine needle aspiration (FNA) of liver in diagnosing hepatocellular carcinoma and liver metastases is proven to be a safe, sensitive and specific method when guided by ultrasound (US) or computed tomography (CT). Numerous studies have reported a sensitivity between 67% and 100% and accuracy rate as high as 96%.[1] This diagnostic method was first applied to the liver as early as 1895. FNA is used predominantly for diagnosing mass lesions when there is a question of a neoplastic process, either primary or metastatic. The procedure, however, has not been successful in identifying diffuse liver disorders, such as hepatitis or cirrhosis. The risk of malignancy growing along the biopsy tract is small but real, with a reported incidence up to 1:1,000 in abdominal biopsies. Severe complications and mortality rate are low, and was reported in 0.04% to 0.05% and 0.004% to 0.008% respectively in two large reviews which included a combined total of more than 65,000 abdominal biopsies.[2]

In most cases, the diagnosis presents no significant challenges to the pathologist. Problems tend to occur when the lesion is a very well differentiated hepatocellular process, which the pathologist must identify as benign or malignant or a poorly differentiated neoplasm that arises in a patient without any other known malignancy, for which the pathologist must determine if it is a primary or metastatic lesion.

Hepatic masses are increasingly being detected on radiography with the use of sophisticated abdominal imaging studies. Specific diagnoses can often be suspected based on sensitive radiographic imaging techniques (computed tomography, magnetic resonance imaging) coupled with clinical data and blood investigations. Except for hemangiomas, however, histopathological diagnosis remains the gold standard in determining tumor classification and appropriate clinical treatment.

The varied array of primary benign and malignant masses and the high rates of metastases to the liver account for much of the diagnostic difficulty encountered. Primary tumors can be solid or cystic and can arise from epithelium (hepatocyte, bile duct epithelium, neuroendocrine cells) or mesenchymal cells (principally endothelium), or heterotopic tissues. The majority of malignant hepatic neoplasms in normal liver represent metastatic carcinoma derived from virtually any primary site, whereas in patients with cirrhosis, hepatocellular carcinoma (HCC) is more common.

Although diagnosis of the primary hepatic neoplasms is often straightforward in resection specimens, definitive classification of a biopsy specimen (core or fine-needle aspiration) showing evidence of benign-appearing hepatocytes can be quite difficult. The most common problem encountered in biopsy specimens is in making the distinction between HCC and metastatic carcinoma. The selective use of immunohistochemistry can be quite useful in this situation.

Since fine-needle aspiration (FNA) has assumed a primary diagnostic role in the evaluation of hepatic masses, this prospective study has been done focussing on the value of percutaneous FNA in the diagnosis of focal liver lesions and their radiological and histological correlation .

AIM OF STUDY

1. To investigate the value of percutaneous FNA in the diagnosis of liver tumors.

2. To evaluate the correlation of FNA diagnosis of focal liver lesions with that of radiological and histopathological diagnosis.

3. To predict the possible primary site in cases of metastatic neoplasm to the liver.

4. To confirm the diagnosis of metastases from a known primary site.

5. To evaluate the role of immunohistochemistry on selected problematic cases.

6. To determine the sensitivity and specificity of cytological diagnosis

REVIEW OF LITERATURE

HISTORY

Hepatic aspiration was performed as long ago as in 1833, when Robert and Biet reported its use in the treatment of hepatic suppuration and hydatid disease.[3,4]

Needle biopsy using aspiration was first employed in 1883 by Paul Ehrlich (cited in Schupfer 1907) in a study of glycogen content of diabetic liver. [5]

Aspiration using very fine needle to evaluate cytological specimens was first used by Lucatello in 1895 (cited in Lundquist 1971).[6] At the beginning of 20th century , needle biopsy was accompanied by a high mortality rate. In 1935 Frola in France tried to reduce complications by using a needle which measured 0.5mm in diameter. Since then in 1939 Iverson and Roholm from Denmark, Baron from USA and other workers from northern continental Europe investigated on cytological methods.[7]

In 1966, Nils So Derstrom [8] published a series of samples in which his observation on metastatic carcinoma and myeloid metaplasia was helpful in clinical diagnosis. Lundquist published several papers including a thesis on his experience of intrahepatic tumors, acute hepatitis, cirrhosis, iron overload, fatty infiltration and other conditions.

In 1967, Sherlock et al [9] proved that more neoplasms are detected when cytological examination is performed in addition to histology. This included fluid from needles and syringes and touch preparations of biopsy tissue.

In 1972, Rasmussen et al[10] described a method for FNA of liver metastases under direct guidance by ultrasonic scanning. They found that FNA cytology had a higher diagnostic rate than routine liver biopsy using the Menghini method.

In 1976, Haaga et al [11] described a method for precise localization of lesion by US/CT. This allowed accurate positioning of needle when lesions were very small and reduced the rate of false negativity. Over the last 15 to 20 years of the 20th century, it became increasingly clear that percutaneous FNA of single or multiple focal liver lesions demonstrated by palpation, nuclear scan , U/S or CT is both accurate and safe .[12,13]

Caution should be exerted when taking a biopsy in a patient with an obstructive biliary tree due to the increased risk of bile leakage. Ascites has also been considered a relative contraindication to biopsy. However, in a comparative study, Murphy et al (1988) concluded that the risk is not higher than biopsies done in its absence.

ALGORITHMIC APPROACH TO FOCAL LIVER LESIONS

1. Establish category of clinical presentation
2. Establish category of radiological findings
3. Establish nature of FNA findings
4. Further confirm nature of FNA findings by Histopathological examination(HPE)
5. Establish final diagnosis based on multidisciplinary approach

1. CLINICAL DIAGNOSIS

The clinical diagnosis of a patient presenting with a liver mass rests on clinical examination of the patient and investigations like hematological analysis including coagulation profile, urine tests, liver function tests, viral markers, serum alpha-fetoprotein (AFP) and evaluation for cirrhosis and biliary tract disease. The clinical diagnosis of malignancy was 58% according to D.K. Das.[14]

2. RADIOLOGICAL FINDINGS

The clinical diagnosis of malignancy improved with imaging.[14] Radiological correlation of liver masses by various imaging techniques like Ultrasonogram (US), Computerised Tomography (CT) and Magnetic

Resonance Imaging (MRI) have assumed a primary role in the evaluation of hepatic masses. The imaging findings of various common focal liver lesions are discussed below . These may be unifocal or multifocal and solid or cystic.

Hepatocellular carcinoma

Ultrasound shows focal form of HCC as a rounded or lobular lesion with often high level echoes and becoming heterogenous with enlargement. Invasion of hepatic veins or portal veins are demonstrated as echogenic foci within the vessel. On non-contrast CT, HCC appears as a solitary mass or multiple masses that are hypodense relative to normal hepatic parenchyma. Calcification is seen in less than 10%. Following administration of intravenous contrast, HCC is normally hyperdense in arterial phase due to its vascularity and hypo or isodense compared to hepatic parenchyma in portal phase. Multifocal HCC appears as low density lesion in unenhanced CT, showing peripheral enhancement and heterogenous internal density on contrast.[15]

Fibrolamellar hepatocellular carcinoma:

On CT, appears as large well defined low attenuation mass. The central stellate scar shows lower attenuation appearance with calcification occurring within the scar. After IV contrast administration, enhancement of tumor occurs because of its perivascularity. A distinguishing feature from HCC is its lack of hemorrhage and necrosis.

Intrahepatic cholangiocarcinoma:

It is an adenocarcinoma arising from small intrahepatic ducts. Ultrasonography demonstrates mass with irregular margins that is slightly hyperechoeic due to fibrotic tissue. CT shows a hypo attenuating mass with irregular margins that shows mild peripheral enhancement. Slow diffusion of contrast medium from vascular to interstitial space results in delayed and prolonged enhancement.

Metastases:

The liver is second in frequency to the lungs as a site of involvement by distant metastases. Although presence of multiple hepatic masses is suggestive of metastatic disease, a variety of benign hepatic lesions can be multiple like cysts, hemangiomas, biliary hamartomas, fungal abscesses and multicentric HCC. On ultrasound, they may be echopoor or echogenic, while mixed patterns as well as fluid regions following necrosis also occur. Metastases are exclusively supplied by hepatic artery. Echogenic lesions are typical of secondaries from urogenital and gastrointestinal tract.

On CT, most metastases are hypervascular and appear hypodense relative to normal liver, that shows rim enhancement representing vascularized viable tumor periphery. Centrally low attenuation may be present if a lesion has central necrosis or cystic change .The borders of metastases may be sharply defined, ill defined or nodular and portal vein invasion is best displayed after

intravenous contrast administration. Hyperdense metastases are usually hyper vascular in nature that appears as a hyper attenuating lesion.[16] Some metastases may have a cystic appearance as seen with mucinous adenocarcinoma of the colon and cystadenocarcinoma of the ovary. In many instances, a preoperative diagnosis can be achieved with a high degree of accuracy based on non-invasive imaging techniques and close clinical correlation. The solid or cystic nature of the lesion, number, size and location of the lesions, absence or presence of hepatomegaly, cirrhosis, steatosis, regional lymphadenopathy and calculi and status of the biliary tract are important clues to the final diagnosis. FNA is useful in defining those lesions without characteristic imaging appearance.

Hepatic adenoma

Ultrasound appearance is often non-specific and mimics other benign and malignant lesions. It appears as a well demarcated hyperechoeic mass. Heterogenous echogenicity may result from hemorrhage or necrosis. Non contrast CT shows well demarcated, hypodense lesions, although hemorrhage and necrosis result in hyperdense lesion. On contrast, early phase peripheral enhancement with subsequent centripetal contrast flow is seen.

3. FINE NEEDLE ASPIRATION FINDINGS

Liver aspirates can come from malignant or benign conditions of hepatocellular or non-hepatocellular origin.

FNA of normal/reactive liver

The liver parenchyma comprises a heterogeneous population of hepatobiliary and related cells, namely, hepatocytes, bile duct epithelium, Kupffer, endothelial, mesothelial and inflammatory cells.[17] Hepatocytes often contain intracytoplasmic inclusions such as fat vacuoles, Mallory bodies and hyaline bodies; as well as intranuclear cytoplasmic inclusions. Pigments such as lipofuscin, bile and iron may be present.

FNA of liver cell dysplasia

Hepatocytes with large cell change, exhibit both cell and nuclear enlargement with nuclear atypia but retaining the normal nuclear-cytoplasmic ratio (N/C) of $\leq 1/3$. On the other hand, in small cell change, with precancerous link to HCC, the hepatocytes are small and monotonous with subtle increase in N/C ratio.

FNA of Hepatocellular carcinoma

With regard to HCC, FNA is accurate with a sensitivity rate of 80 to 95% and a specificity rate of 100%.[18,19,20]

Needle aspiration biopsy may occasionally be used as an additional staging procedure to distinguish tumor invasion in the portal vein from simple thrombus.[21]

The sensitivity of guided FNA for diagnosing hepatic malignancy in most recent series is 90% to 96%, with a specificity of 90% to 100%. False-negative diagnoses of HCC are related either to very well differentiated tumors that are difficult to identify on the basis of cytology as being neoplastic or to poorly differentiated tumors that are difficult to distinguish as hepatocellular in origin.

The presence of at least two of three criteria (polygonal cells with centrally placed nuclei, malignant cells separated by sinusoidal endothelial cells and bile) was considered by Bottles et al[21] to be 97% sensitive and 100% specific for HCC compared with other malignancies. Cohen et al[22] found that the presence of the following three features was 87% specific and 100% sensitive for the diagnosis of HCC versus non neoplastic conditions: an increased nuclear to cytoplasmic ratio, a trabecular pattern and atypical naked nuclei.

Classic HCC is usually graded into well, moderately or poorly differentiated lesions. Histologic patterns comprise trabecular-sinusoidal, pseudoacinar and solid types; combinations are frequent.

CYTOLOGICAL FEATURES

- Hypercellular smears with uniformly granular pattern of spread of the cells.

- Cohesive clusters of malignant hepatocytes with arborizing, tongue-like projections of broad cords (>2 cells thick) that may be wrapped by peripheral endothelium.

- Rows of transgressing endothelium in larger aggregates, “sinusoidal capillarization".[23]

- Pseudoacini containing bile or pale secretions .

- Hepatocytic characteristics include polygonal cells with well-defined borders, ample granular cytoplasm, central round nucleus, well-delineated nuclear membrane, prominent nucleolus and fine, irregularly granular chromatin. Mitoses increase with nuclear grade.

- Well differentiated HCC cells tend to be conspicuous by their small size, monotony, subtle increase in N/C ratio and nuclear crowding. Poorly differentiated HCC cells tend to be pleomorphic.

- Atypical naked hepatocytic nuclei are seen.

- Bile may be present within tumor cells or in canaliculi or pseudoacini.

- Intracytoplasmic fat and glycogen vacuoles are common. Intracytoplasmic inclusions include hyaline, pale and Mallory bodies. Intranuclear cytoplasmic inclusions are seen.

- Bile duct epithelial cells, if present, are few and far apart. Kupffer cells may be seen.

FNA of variants of hepatocellular carcinoma

The variants of HCC include:

HCC with fatty change; HCC- clear cell type; HCC- small cell type; HCC- undifferentiated type; HCC-spindle cell type; HCC- giant cell type**;** HCC with biliary differentiation.

Fibrolamellar HCC:

This occurs in non-cirrhotic livers of young patients and has a good prognosis. It comprises large, discohesive polygonal hepatocytes with abundant oncocytic cytoplasm and lamellar fibrosis. Pale bodies are common.

Combined hepatocellular-cholangiocarcinoma (CHCC-CC):

This is a rare tumor containing unequivocal elements of HCC and CC that are intimately admixed with a transitional component. The HCC cells are expected to be AFP and Hep Par 1-positive and show polyclonal CEA (*p*CEA) canalicular staining. The CC cells are AE1/3-positive and show brush border/diffuse cytoplasmic *p*CEA reactivity. The intermediate cells exhibit hybrid features with equivocal immunoprofiles.

FNA of cholangiocarcinoma

Intrahepatic Cholangiocarcinoma are rare and usually well to moderately differentiated adenocarcinomas with variable degree of

desmoplasia. Smears are variably cellular and shows sheets or clusters or tubular arrangement of cuboidal to columnar cells with eccentric large regular nuclei & prominent nucleoli. The cytoplasm shows fine vacuolization. The tumor cells are usually loosely cohesive ,and form acini. Hepatocytes are absent.

FNA of metastatic carcinoma

The liver is a common target for metastases. This makes the separation between primary and secondary malignancies all the more difficult, especially when the particular histologic subtype can arise in the liver as well.

- **Adenocarcinoma:** Most are metastases from stomach, colorectum, pancreas, breast and lungs. Colorectal metastases have much tumor diathesis. Signet-ring cell adenocarcinomas are likely to be gastric in origin. Pancreaticobiliary tract adenocarcinomas can have squamous components. For any adenocarcinoma in hepatic aspirates, CC, HCC with pseudoacini and CHCC-CC have to be considered.

- **Squamous cell carcinoma:** Most are metastatic or arise in the pancreaticobiliary tract. Large, spindly, "tadpole-shaped" or bizarre cells with dense cytoplasm, keratinization and much necrosis may be seen.

- **Spindle cell malignancy:** Well-differentiated spindle cell tumors include leiomyosarcoma (LS), neurogenic tumors and

fibroblastic/stromal tumors including gastrointestinal stromal tumor (GIST). At the poorly differentiated end, Leiomyosarcoma, malignant fibrous histiocytoma, undifferentiated sarcoma or even sarcomatoid HCC or CC with a spindle cell component, have to be considered.

- **Others** include Small/intermediate round cell malignancy, Pleomorphic cell malignancy and Clear cell malignancy

FNA of Hepatic Adenoma:

The smears are moderately cellular with monotonous cells resembling normal hepatocytes. The cells are uniform, polygonal with central round nuclei, with low nuclear cytoplasmic ratio. The cytoplasm is usually pale or vacuolated. The absence of bile duct epithelium is of diagnostic significance.

FNA of Hepatoblastoma:

Distinctive finding of FNA of fetal epithelial type includes highly cellular smears with small malignant cells in clusters, rosettes or trabeculae. The nuclei are round to oval and hyperchromatic with occasional nucleoli and scant cytoplasm. The embryonal type shows small oval to spindled cells with round to oval nuclei with prominent nucleoli, high N/C ratio and mitotic activity. Malignant mesenchymal tissue may be present. Extramedullary haemopoiesis is common.

4. HISTOPATHOLOGICAL FINDINGS (HPE)

Histopathology is the gold standard for diagnosis of any malignancy. The histopathological findings of common focal liver lesions are discussed below;

Hepatocellular Carcinoma

Malignant epithelial tumors account for about 98% of all primary hepatic malignancies, with HCC representing by far (about 85–90%) the single most common histologic type. The male-to-female ratio is 3:1 to 6:1. Patients usually show symptoms in the sixth or seventh decade of life.Virtually any condition associated with chronic hepatic injury (usually cirrhosis) may predispose toward HCC; hepatitis B, hepatitis C and alcohol are the other etiologic factors associated with an increased risk of HCC. HCC in the normal liver may also arise from hepatic adenoma or nodular regenerative hyperplasia.

Periodic screening of patients with chronic liver disease for HCC, using a combination of ultrasonography and serum levels of AFP has become an accepted practice by hepatologists and has led to the diagnosis of many small (less than 2 cm) asymptomatic HCCs.

Serum AFP levels remain the most useful marker for HCC. The level of serum des-U-carboxy prothrombin (DCP) has been suggested as an useful marker (60–90% sensitive, 85% specific); tests may be positive in nearly 30%

of AFP-seronegative patients. Serum AFP levels are elevated (more than 10 to 20 ng/ml) in about 70% to 80% of patients(specificity 90%). Sustained AFP increases suggest HCC, but HCC can develop in the absence of elevated serum AFP. Malignant neoplasms often associated with very high levels (more than 1,000 ng/ml) of serum AFP include HCC, HBL, and germ cell tumors containing a yolk sac component.

Small Hepatocellular Carcinoma

Virtually all tumors less than 1 cm consist of Well differentiated HCC with relatively thin trabeculae (less than or equal to three cells thick) of small hepatocytes showing little atypia. WD-HCC is distinguished from borderline foci/nodules, from which it may arise (nodule in a nodule), by a nuclear density greater than twice normal and by mild but definite nuclear atypia and inconspicuous nucleoli. Fatty change is noted in 40% of cases, sometimes with Mallory bodies. Stromal and portal tract invasion may occur, but vascular invasion is quite rare.

Advanced Hepatocellular Carcinoma

The tumor cells resemble that of normal hepatocytes typically arranged in a trabecular pattern outlined by sinusoids. Histological grading of HCC was devised by Edmundson and Steiner nearly 50 years ago; subsequently, other similar systems have been proposed. Most tumors are moderately differentiated (grades 2 to 3).Without definite evidence of hepatocellular differentiation, a

malignant epithelial tumor in the liver should be regarded as a poorly differentiated carcinoma that is most likely metastatic.

HCC is typically associated with little tumor-induced stroma. Significant fibrosis occurs in about 5% of cases of scirrhous and fibrolamellar variants of HCC. As HCC progresses from a small to an advanced type, the extent of sinusoidal capillarization increases. The World Health Organization (WHO) recognizes five histological patterns and four cytological variants of HCC.

Histological Patterns; These patterns are frequently found together in the same tumor. Only the fibrolamellar type appears to have prognostic significance. The patterns are

1. Trabecular or sinusoidal

2. Compact or solid

3. Pseudoglandular (acinar, adenoid)

4. Fibrolamellar

5. Scirrhous

Cytological Appearance; The tumor cells are usually polygonal and have (a) distinct cell membranes (b) a higher nuclear to cytoplasmic ratio compared with normal hepatocytes, (c) abundant, finely granular eosinophilic cytoplasm and (d) a round nucleus often containing coarse chromatin and a thickened or

irregular nuclear membrane. Although nucleoli are often prominent, this is not a consistent finding. The cytological variants of HCC include:

1. Pleomorphic or giant cell

2. Clear cell

3. Oncocyte-like

4 .Sarcomatoid or spindle cell

Several different types of eosinophilic hyaline globules, both intra- and extracellular, have been described in 10% to 15% of HCCs. They often display immunoreactivity for AFP, A1AT, or alpha1-antichymotrypsin (A1ACT). The finding of a hepatic tumor with immunoreactivity for AFP is very suggestive of HCC and its presence in poorly differentiated tumors may be of particular diagnostic utility. However, other neoplasms (such as HBL; adenocarcinomas of the pancreas, stomach and lung and yolk sac tumor) may demonstrate this antigen. Measuring serum AFP by modern techniques is more sensitive than finding immunohistochemical evidence of AFP in tumor tissue.

Fibrolamellar Hepatocellular Carcinoma

The tumor consists of large polygonal cells with abundant granular eosinophilic cytoplasm (oncocytes), sharply defined cell borders and a large vesicular nucleus with a prominent nucleolus. These neoplastic hepatocytes are

separated into nests, columns or variably sized sheets by parallel, hyalinized bands of relatively acellular collagen (thus the term “fibrolamellar”) that may contain small, thick-walled arteries. Mitoses are infrequent.

Combined Hepatocellular Carcinoma–Cholangiocarcinoma

Less than 5% of primary hepatic carcinomas demonstrate an intimate admixture of both unequivocal HCC and cholangiocarcinoma (hence combined HCC-CC), the latter characterized by cells with a cuboidal to columnar shape, less abundant and more amphophilic cytoplasm, less conspicuous nucleoli, gland formation and mucin production. Separate HCC and CC, no matter how closely situated in the liver are best considered “collision tumors” rather than combined HCC-CC. A tumor that has foci only suggestive but not diagnostic of both HCC and CC should be considered an undifferentiated carcinoma and is likely a metastasis. A “biliary type” CK profile has been suggested as helpful in defining the cholangiocarcinoma component.

Hepatoblastoma

HBL represents the most common primary hepatic tumor in children. The serum AFP level is elevated in up to 90% of cases, usually with very high titers. HBLs may be classified as either epithelial (56%) or mixed epithelial–mesenchymal (44%). The epithelial component is usually divided into irregular lobules by collagenous septa. Foci of extramedullary hematopoiesis may be found in the sinusoids of either the fetal or the embryonal patterns.

1. Fetal pattern (31%): In this pattern the hepatocytes are similar in size to or smaller than those seen in the adjacent non neoplastic liver. They have a slightly higher nuclear to cytoplasmic ratio and inconspicuous nucleoli. The tumor cells are arranged in trabeculae two to three cells thick, separated by sinusoids lined by endothelial cells. Portal tracts, bile ducts and ductules are absent.

2. Embryonal pattern (19%): Compared with the fetal pattern, the tumor cells have more poorly defined cell borders, more basophilic cytoplasm, a higher nuclear to cytoplasmic ratio, coarser chromatin, and more prominent nucleoli.

3. Macrotrabecular pattern (3%): This pattern is characterized by trabeculae that are ten or more cells.

4. Small-cell undifferentiated pattern (3%).

5. Mixed epithelial and mesenchymal pattern (44%):The primitive mesenchymal component has oval to spindle-shaped cells with little cytoplasm, often located within or adjacent to the neoplastic epithelial component.

Intrahepatic Cholangiocarcinoma

Microscopic Features: Most cases of CC demonstrate a variable degree of glandular (ductal, tubular) differentiation and mucin production with a

moderate amount of densely fibrotic stroma. In well-differentiated cases, the glands are lined by cuboidal to low columnar cells that contain a moderate amount of pale sometimes slightly granular cytoplasm. The size of the cells and nuclei is generally smaller and the nucleoli less prominent than in HCC. Bile is not produced by cholangiocarcinomas. A trabecular pattern may be found simulating HCC, but collagenous stroma, rather than sinusoids surround the cords of tumor cells; bile canaliculi as well as bile are absent.

Making the distinction between cholangiocarcinlma and metastatic adenocarcinoma, particularly from the gallbladder, pancreas, extrahepatic biliary tree and breast is impossible on histological grounds. At present, there are no specific tumor markers useful in distinguishing cholangiocarcinoma from other forms of adenocarcinoma.

Metastatic tumors in the liver

Metastatic tumor accounts for about 98% of all hepatic malignancies and is found in nearly 4% of all liver biopsies. Forty percent of patients dying from cancer have hepatic metastases. In the cirrhotic liver, however, primary hepatic malignancies (nearly always HCC) are more common than metastatic tumors representing 77% and 23% of all hepatic malignancies respectively . The sensitivity of ultrasonography and CT for detecting metastatic disease is about 85% but it is considerably lower when lesions are few and smaller than 2 cm. Carcinomas of the lung, breast, colon and pancreas account for the

overwhelming majority of hepatic metastases in adults, whereas metastatic neuroblastoma, Wilms' tumor, and rhabdomyosarcoma are most common in the pediatric age group. Carcinomas of the pancreas, stomach and lung are the tumors most likely to be found in adults in conjunction with hepatic metastases and an inapparent primary site. In general, patients with hepatic metastases die within 1 year, but notable exceptions include patients with metastatic neuroendocrine neoplasms and neuroblastoma and a select subgroup (approximately 5%) of patients with metastatic colon carcinoma. In the latter instance, 5-year survival rates of 25% to 39% have been reported after resection of hepatic metastases.

Hepatic Adenoma (HCA)

Microscopic Features include normal-sized or slightly enlarged hepatocytes in cords that are one to two cells thick. Bile ducts, ductules and portal tracts are absent within HCA. The hepatocytes of HCA possess acidophilic, clear or vacuolated cytoplasm. The nuclei are bland with inconspicuous nucleoli. The so-called oncocytic liver cell adenoma may represent an oncocytic variant of HCC.

The absence of a classic trabecular pattern, a relatively low nuclear to cytoplasmic ratio and the absence of vascular invasion aid in making the histopathologic distinction from HCC.

5. FINAL DIAGNOSIS BASED ON MULTIDISCIPLINARY APPROACH

Close clinicopathological correlation is mandatory for enhancing the yield of FNA diagnoses and the reduction of indeterminate reports. A benign cytodiagnosis obviates unnecessary surgery. Surgical resection is indicated for any resectable malignant hepatic mass be it primary or secondary. In unresectable malignant lesions, a precise cytohistological typing is crucial for appropriate alternative therapy. There is no reliable data to establish the risk of needle track seeding. Only 0.006% has been regarded by many authors.[24,25,26] Tissue procurement by FNA under radiological guidance and cytological interpretation of the aspirated material has improved the diagnosis of malignnacies of the liver.

FINE NEEDLE ASPIRATION VERSUS CORE NEEDLE BIOPSY

Fine needle aspiration :

Fine needle aspiration is useful for (i) cirrhotic patients with poor liver function with risk of bleeding; (ii) liver masses with obstructive jaundice and risk of bile leakage, those near big vessels, or where there is need to go through bowel; (iii) small (<2 cm diameter), deep-seated and difficult to approach nodules that require close patient co-operation during the procedure; (iv) representative sampling of sizeable lesions by re-direction of the needle and multiple passes and (v) on-site rapid assessment of adequacy and rendering of

provisional diagnosis, as well as for appropriate triage of tissue specimens for ancillary studies (e.g. microbiology, flow cytometry, genetic testing, molecular diagnostics, cell block preparation and electron microscopy).

Core needle biopsy:

Core needle biopsy, with the availability of more material, provides tissue for histological and immunohistochemical studies, especially in two major areas of diagnostic difficulties namely in the (i) differentiation of well differentiated HCC from benign hepatocellular nodules; and (ii) separation of HCC from Cholangio carcinoma and metastases.

Consensus: The diagnostic accuracy in terms of sensitivity, specificity and positive predictive value of FNA for HCC is almost similar to that of core needle biopsy. The accuracy rate is highly operator-dependent and increases with both techniques combined. The specificity and positive predictive value of FNA in the diagnosis of malignant hepatic lesions has been shown to be close to 100% in most studies.[27,28,29,30] These results are comparable to the accuracy of core needle biopsy. In a comparative study, it was reported that both procedures FNA and core needle biopsy, had the same diagnostic accuracy of 78% when considered separately and of 88% when considered in combination.[31] The conclusion was that the great advantage of combining the two techniques was the reduction in false negative results. Using larger caliber cutting needle, biopsies can be associated with a greater number of

complications.[30] Many studies have shown improved diagnostic yield and accuracy of FNA using the combined cytohistological approach.[32,33]

FNA can provide rapid on-site diagnosis when the smears are stained with Diff-Quik or Ultra-fast Papanicolaou stain.[34] In the era of rising costs in medical practice and higher patient/practitioner/institution expectations of efficiency and faster turn-around time, FNA can obviate the need to wait for tissue processing if accurate cytological diagnoses can be rendered. Another cost-saving advantage, especially for less developed countries is that smears are cheap, convenient and easy to prepare as long as there is an experienced person to interpret them.

Considering the overall advantages and cost-analysis, FNA can be suggested as the initial method of choice for evaluation of focal liver lesions in most clinical settings.

Diagnostic utility of immunohistochemistry

There are two major applications for immunohistochemical markers in the diagnostic workup of focal liver lesions. One is to decipher the exact histogenetic origin of obvious tumor nodules i.e the histological typing and the primary site. It may not always be possible to distinguish between the poorly differentiated entities of HCC, cholangiocarcinoma and metastatic carcinomas. Adenocarcinomas occurring in the liver may be metastatic or primary in origin. Of interest lately is the increasing documentation of AFP-producing

extrahepatic hepatoid/non-hepatoid carcinomas that have a propensity for vascular invasion and liver metastases. The immunoprofile of these tumors, originating mostly in the GIT and lungs, is almost identical to that of HCC. Serum AFP levels tend to be very high. For ascertainment of malignancy in hepatocellular nodules, the antibody panel should comprise at least AFP, *p*CEA or CD10, and CD34.[35,36,37] The panel should comprise at least AFP, *p*CEA or CD10, and CD34.[35,36,37]

- **CD10** should be included if the histogenesis of the tumor is to be studied. The sensitivity of CD10 (68.3%) is far better than immuno-staining for AFP (23.8%) but less sensitive than *p*CEA (95.2%) in the diagnosis of HCC

- **AFP** is fairly specific but not sensitive for HCC. Tissue AFP immunoreactivity is expected in HCC but it may be patchy and minimal. Sensitivity is about 50% (range, 20–75%) and is low at both ends of the histologic spectrum of HCC. A study of 56 patients with small HCC (<2 cm diameter) showed AFP-positivity in 44.6% of the tumors. A variable staining pattern may be encountered with CHCC-CC.

- ***p*CEA**. There are two patterns of staining in HCC – canalicular and/or diffuse cytoplasmic staining. Bile located within neoplastic cells or tubular lumina is pathognomonic of HCC. Routine immunohistochemical testing using unabsorbed polyclonal anti-CEA

antiserum or certain monoclonal CEA (m-CEA) antibodies, each of which cross-reacts with canalicular biliary glycoprotein 1, demonstrates bile canaliculi (canalicular pattern) in 70% to 80% of HCCs.

Canalicular CEA staining remains the most useful and most thoroughly investigated immunohistochemical marker in the differential diagnosis of HCC, although one drawback is that about 50% of poorly differentiated tumors lack immunoreactivity.

- **Hep Par 1 (Hepatocyte antigen)** Hep Par-1 is a recently described monoclonal antibody that reacts with a hepatocyte-specific epitope, the exact nature of which is unknown. Its staining pattern suggests organelle localization, possibly mitochondrial . Studies from the University of Pittsburgh have shown performance characteristics similar to p-CEA with 82% sensitivity and 90% specificity. Drawbacks to the use of this antibody are that it is not commercially available, occasional staining of non-HCC malignancies has been described and that there are false positives due to staining of trapped non neoplastic hepatocytes and insensitivity of identification of poorly differentiated HCC (50%) However, not all HCC stain uniformly and not all Hep Par 1-positive tumors are of hepatocellular origin or arise in the liver. MRN, DN, FNH and LCA tend to exhibit 100% positivity. Hence, this antibody has no discriminant value in the evaluation of the biological status of well-differentiated hepatocellular nodular lesions.

- **Cytokeratins** (CK 7, 8, 18, 19, 20; CAM 5.2; AE1/AE3). Mature hepatocytes stain with CK 8 and 18 and CAM 5.2 but not with CK 7, 19 or 20 or AE1/AE3.Bile ducts express CK 7 and 19. CAM 5.2 is the most reliable cytokeratin antibody for HCC. AE1/AE3 negativity is expected in hepatocellular lesions. Focal CK 7 and 19 positivity can be seen in high-grade HCC. HCC is generally CK 20 negative. HCCs (up to 60%, particularly moderate and poorly differentiated tumors) and even non neoplastic hepatocytes have been found to frequently modify their CK expression and express non hepatocyte CK (other than CK 8 and 18) therefore limiting their diagnostic utility

- **CD34** highlights regions of sinusoidal capillarization where there is basement membrane material deposition. Diffuse sinusoidal CD34 reactivity is seen in HCC, even in small WD-HCC. However, significant reactivity is also seen in LCA and some FNH.

- **Erythropoiesis-associated antigen (ERY-1**; not commercially available) was found in 89% of HCCs in one study is a sensitive marker for hepatocytic differentiation and is part of the antibody panel for distinguishing HCC from CC and metastases

In summary, many investigators currently use a panel of p-CEA (canalicular pattern), m-CEA and AFP antibodies when evaluating diagnostically challenging cases. HepPar-1 and ERY-1 may prove to complement and enhance the performance characteristics of this approach.

MATERIALS AND METHODS

This prospective study was undertaken in the Institute of Pathology, Madras Medical College from June 2006 to July 2008. Fifty two patients who were detected to have focal liver lesions by US/CT imaging were chosen and subjected to FNA followed by trucut biopsy under US guidance. The aspirations were performed either to confirm or exclude suspected primary or metastatic liver malignancy based on clinical findings in symptomatic patients. All patients signed informed consent prior to aspiration and the study protocol conformed to the ethical guidelines of the Declaration of Government General Hospital, as reflected in a prior approval by the Hospital's Human Research Committee.

Inclusion and exclusion criteria were used to select the patients for interventional procedure.

INCLUSION CRITERIA:

Candidates for liver biopsy must be carefully selected, as this procedure, by nature, is invasive. In all cases, noninvasive imaging studies such as CT scan or ultrasound are obtained first. Though there are many indications for liver biopsy, this prospective study focusses on the radiologically (CT/US) proven cases of focal liver lesions.

EXCLUSION CRITERIA

1. Impaired hemostasis with prothrombin time more than 3 seconds over control, PTT more than 20 seconds over control, thrombocytopenia and markedly prolonged bleeding time (Mahal et al[38] in 1979 noted 22 bleeding episodes in3800 percutaneous liver biopsies)
2. Severe anemia (Hb <8 g/dL)
3. Local infection near needle entry site, such as right sided pleural effusion or empyema, right lower lobe pneumonia, local cellulitis, infected ascites or peritonitis
4. Tense ascites (low yield technically, risk of leakage)5. High-grade extrahepatic biliary obstruction with jaundice (increased risk of bile peritonitis)
5. Septic cholangitis
6. Possible hemangioma
7. Possible echinococcal (hydatid) cyst
8. Uncooperative patient
9. Poor performance status
10. Advanced malignancy

PATIENT PREPARATION:

Procedures and risks of the procedure were explained and informed consent was obtained. Procedure entailed overnight hospitalization and the patients needed to stay in the hospital for 1-2 days post biopsy for observation. All aspirin products and non steroidal agents were discontinued at least 5 days beforehand. Injection vitamin K was given in jaundiced and liver failure patients. The patients were kept in empty stomach after midnight, the day prior to the procedure. Screening laboratory studies including CBC, PT/PTT, BUN, bleeding time, coagulation time and typing and crossmatching for possible transfusion, electrolytes and liver function tests, viral markers and serum alpha feto protein were done 24-48 hours in advance.

EQUIPMENT: Disposable automated Trucut biopsy gun –18 Gauge needle with 2 cm throw length, designed to cut out cores of tissue. Specimens obtained with this needle were less fragmented, even in the cirrhotic liver and thus a high success rate. Specimen was obtained using suction/aspiration into a 10 ml syringe. Trucut needle is a modernized Vim-Silverman needle.

TECHNIQUE:

Patient was laid supine in bed with right hand behind his head. Liver margins were estimated by ultrasound. Two approaches are popular, transthoracic (intercostal) or subcostal (anterior). With the former, biopsy site is identified along the midaxillary line in the center of hepatic dullness, usually

the eighth or ninth intercostal space.This approach avoids other abdominal organs but always penetrates the pleura.With the subcostal approach, the biopsy site lies below the bottom rib anteriorly and is used when a liver mass is easily palpable below the right costal margin. The risk of visceral laceration is higher and this approach is infrequently used.

A wide area was prepped and draped in sterile fashion. The skin was anaesthetized with 1% lidocaine, then deeper structures such as subcutaneous tissue, intercostal muscles and diaphragm were infiltrated in that order. A small superficial incision was made with a No 11 blade at the needle entry site to facilitate needle insertion. The first needle pass should sample the centre of the lesion since this will reduce contamination by cells from surrounding normal liver. The centres of large lesions may occasionally be necrotic and hence may not render diagnostic material. If the first pass yielded only necrotic debris and/or inflammatory cells, the second pass should be made close to the edge but well within the target. Under US guidance, an outer guide needle of larger diameter and 10 cm long was first introduced through the superficial layers. This outer needle will not only ensure needle stability, but will also allow multiple passes of the needle without inconvenience to the patient. The fine needle of 20 gauge was attached to a disposable syringe and was passed through it. When the tip of the fine needle was correctly located within the lesion by US, negative pressure was applied and the needle advanced steadily for 1-2 cm and moved back and forth. With the needle still in position negative

pressure was released and needle withdrawn. The patient was asked to suspend respiration during advancement of the needle. Usually several passes of the needle were performed in slightly different directions to ensure representative sampling. The material in the needle was expelled on to glass slides and smeared immediately.

Through the outer needle, 18 gauge automated biopsy gun of 2 cm throw length was inserted and patient asked to suspend respiration. The position of the stylet was confirmed by US and then the device was fired. A 2.5 cm core of liver was aspirated and needle withdrawn. Several passes of the biopsy needle (2-3) were performed to minimize sampling bias.

SPECIMEN:

At least two to three liver cores, each more than 2 cm in length was routinely fixed in 10% buffered formalin, specimen processed and the tissues stained with hematoxylin and eosin.

Cytological preparation - fluid from aspirating syringe was smeared on clean microscope slides and sent to Cytology Laboratory.Smears were air-dried and stained with May-Grunwald-Giemsa as well as fixed in 95% alcohol and stained by the Papanicolaou method and hematoxylin and eosin.

AFTERCARE:

Patients were monitored in a recovery area with frequent examination of vital signs (blood pressure, pulse) post biopsy. If no complications were apparent, they were transferred back to ward in stretcher. Strict bed rest was enforced for 24 hours. For the first 2 hours, patient was positioned on his right side. Vital signs were checked frequently. Diet was restricted to clear liquids for several hours, then full liquids as tolerated. Acetaminophen was usually sufficient for pain control.

COMPLICATIONS:

Based on several large series, serious morbidity has been estimated at 0.1% to 0.2%. Fatality rates have ranged from 0% to 0.17%, both figures being derived from studies involving >20,000 biopsies each. The more commonly seen complications are:

1. Pain was the most common adverse event, noted in almost all the cases.

2. Hemorrhage - minor episodes were common. Self-limited oozing from the puncture site persisted for approximately 1 minute, but with loss of only 5-10 ml blood. Significant hemorrhage was less frequent. But is the most common cause of death from liver biopsy. Several series have estimated an incidence of approximately 0.2%, but Sherlock (1984) reported 40 patients out of 6379 required transfusion for intraperitoneal

bleeding.[39] Bleeding usually results from a tear of a distended portal or hepatic vein and vascularized tumor. In our study we did not encounter any massive bleeding episodes.

3. Bile leakage with peritonitis - associated with severe obstruction of the larger bile ducts. This is felt to result from laceration of a small, distended duct or from puncture of the gallbladder.

4. Laceration of internal organs and viscera

5. Others: right-sided pneumothorax.

RESULTS

This prospective analysis was done on fifty two patients, among which 39 were males accounting to 75% of our study population with focal liver lesions and 13 were females which was 25% (Table 1)

Table 1 : STUDY POPULATION – SEX DISTRIBUTION

	Male	Female
Number of cases	39	13
Percentage of total	75%	25%

The peak incidence of focal liver lesions was highest in the age group of 61-70 years in the males and 41-50 years in the females as given in Table 2 and figure 2.

Table 2 : STUDY POPULATION – AGE & SEX DISTRIBUTION

AGE (YRS)	MALE	FEMALE	TOTAL
1-10	1	1	2
11-20	0	0	0
21-30	1	0	1
31-40	5	4	9
41-50	3	5	8
51-60	11	1	12
61-70	16	2	18
71-80	2	0	2
TOTAL	39	13	52

Fig.1

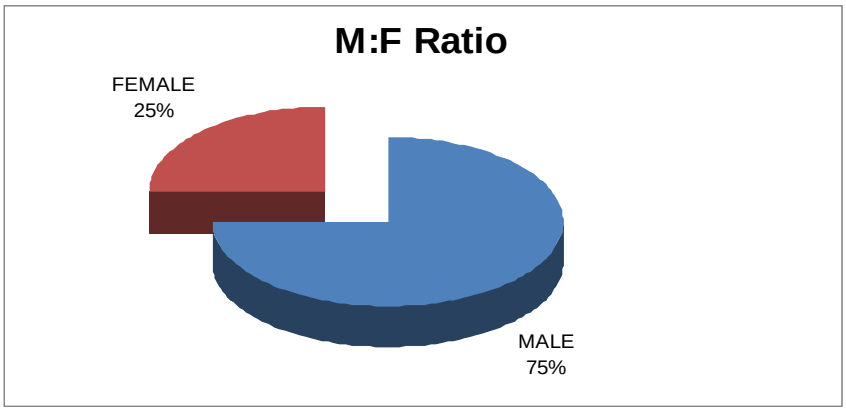
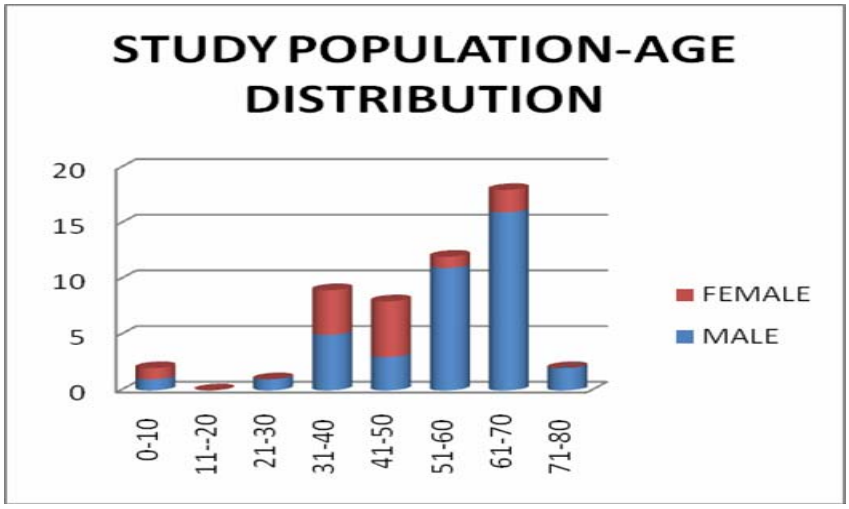

M:F Ratio
FEMALE
25%
MALE
75%

Fig.2


STUDY POPULATION-AGE DISTRIBUTION
20
15
10
5
0
0-10
11--20
21-30
31-40
41-50
51-60
61-70
71-80
FEMALE
MALE

Males formed the majority of the cases reported as Hepatocellular carcinoma contributing to 20 of the 24 cases of which 45% were in the sixth decade as shown in table 3. The incidence of liver secondaries was also high in males (14 cases) and in seventh decade, as that of hepatocellular carcinoma.as shown in table 4.

Table 3 : HEPATOCELLULAR CARCINOMA- AGE & SEX DISTRIBUTION

AGE (YEARS)	MALE	FEMALE	TOTAL
31-40	2	2	4
41-50	2	2	4
51-60	9	0	9
61-70	6	0	6
71-80	1	0	1
TOTAL	20	4	24

Table 4 : LIVER SECONDARIES – AGE & SEX DISTRIBUTION

AGE (YEARS)	MALE	FEMALE	TOTAL
31-40	3	2	5
41-50	1	3	4
51-60	2	0	2
61-70	8	1	9
TOTAL	14	6	20

Fig 3

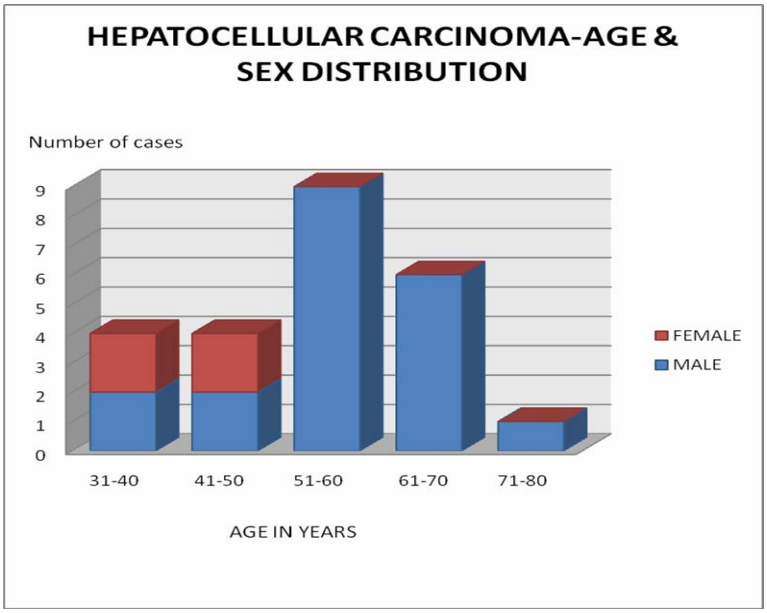

HEPATOCELLULAR CARCINOMA-AGE & SEX DISTRIBUTION
Number of cases
9
8
7
6
5
4
3
2
1
0
31-40
41-50
51-60
61-70
71-80
AGE IN YEARS
FEMALE
MALE

Fig 4


LIVER SECONDARIES-AGE & SEX DISTRIBUTION
Age in yrs
61-70
51-60
41-50
31-40
0
2
4
6
8
10
MALE
FEMALE

The damage to the liver by various focal lesions was clinically manifested as jaundice in 12cases (23%), liver failure in 6 cases (11.5%), portal hypertension in 10 cases (19.2%), loss of weight and loss of appetite in 23 cases (44.2%). Similar results were found in both HCC and metastatic liver lesions.

Table 5 : STUDY POPULATION – CLINICAL MANIFESTATIONS

Clinical features	Number of cases	%
Jaundice	12	23.08
Liver failure	6	11.54
Portal Hypertension	10	19.23
Loss of appetite/Loss of weight	23	44.23

Fig 5

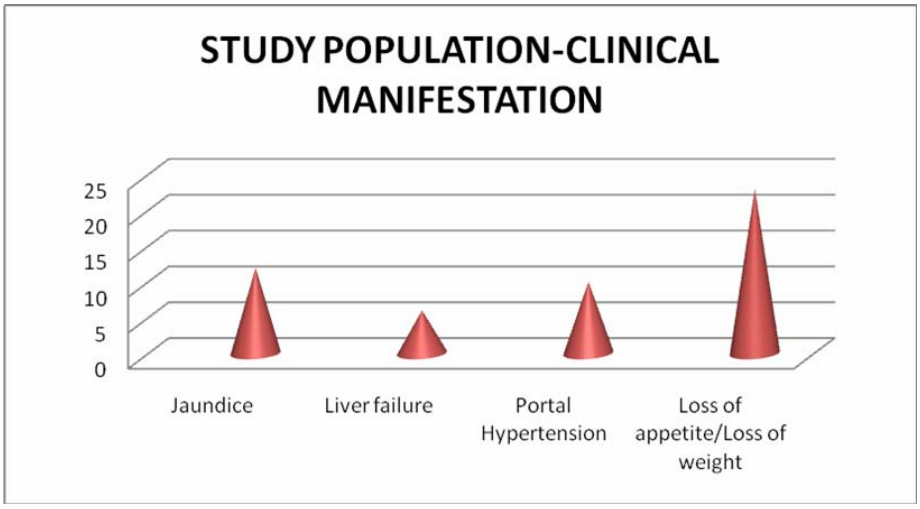


Table 6 : CLINICAL MANIFESTATIONS IN HEPATOCELLULAR CARCINOMA

Clinical features	Number of cases	%
Jaundice	10	19.23
Liver failure	4	7.69
Portal hypertension	9	17.31
Loss of appetite/loss of weight	17	32.69

Fig 6

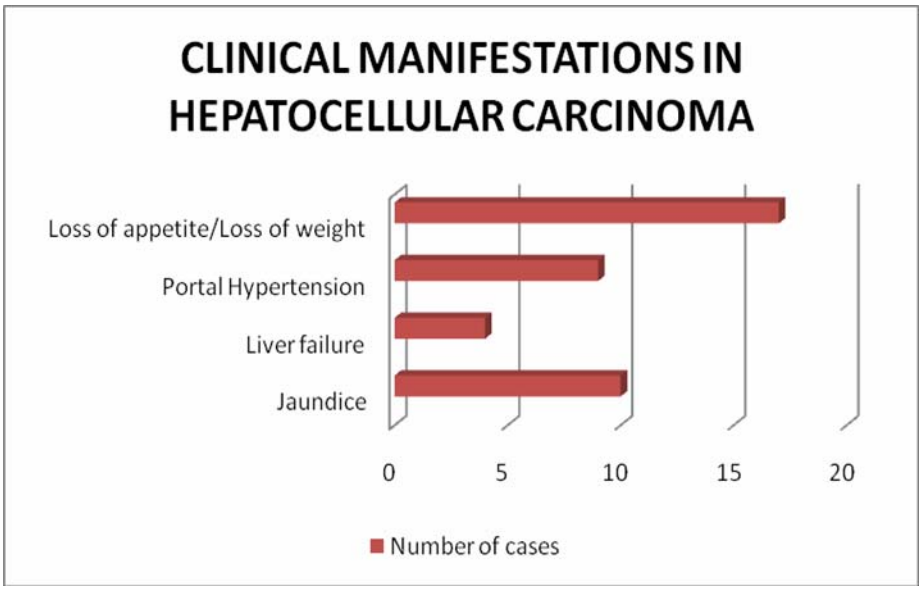


Table 7 : STUDY POPULATION – LAB INVESTIGATIONS

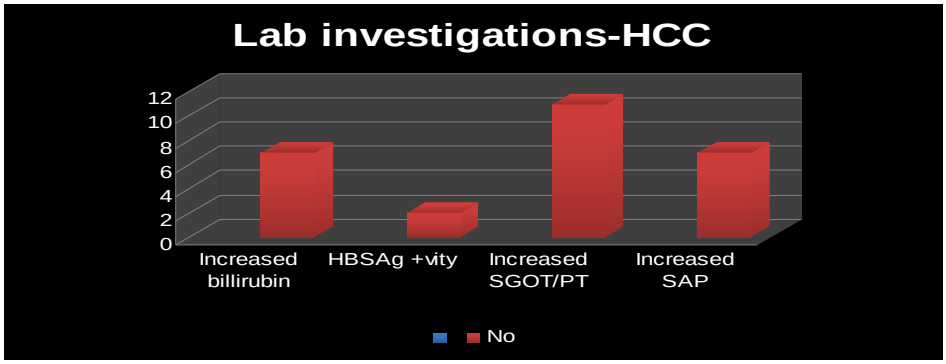
Lab investigations	Number of cases	%
Increased bilirubin	7	13.4
HBS Ag	2	3.85
Increased SGOT/ SGPT	11	21.15
Increased SAP	7	13.4

HBS Ag- Hepatitis B surface antigen

SAP- Serum Alkaline Phosphatase

The abnormalities in liver function tests in our study population are shown in table 7 and figure 7. Increased bilirubin was seen in 7 cases (13.5%), increased SGOT/SGPT in 11 cases (21%) and increased serum alkaline phosphatase in 7 cases (13.5%). Viral markers were done for all cases and 2 cases showed positivity. Similar results were found in both HCC and metastatic liver lesions.

Fig 7

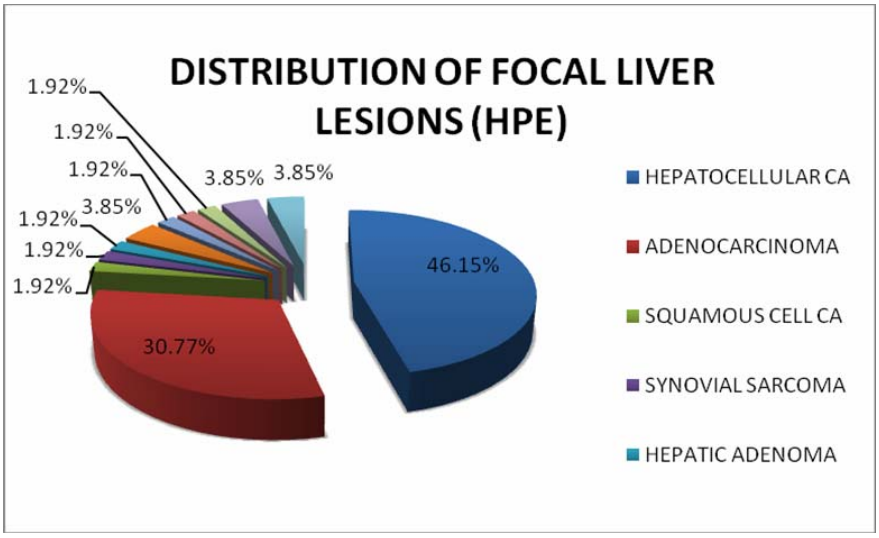


Among the 52 cases of focal liver lesions subjected to US guided FNA and biopsy, histopathological diagnosis was primary hepatocellular carcinoma in 24 cases (46.15%), followed by secondary adenocarcinomatous deposits in 16 cases (30.77%) and hepatoblastoma in 2 cases (3.85%). Other interesting cases were Cholangiocarcinoma (1.92%), hepatic adenoma (1.92%), secondary synovial sarcomatous deposit (1.92%) and secondary squamous cell carcinomatous deposits (1.92%) each contributed to one case. Definitive typing of malignancy could not be done in 2 cases (3.85%), for which immunohistochemistry was done. Biopsy material was inadequate and showed no evidence of malignancy in 2 cases (3.85%). One case showed evidence of liver cell dysplasia (1.92%) only. Another case which had definitive radiological evidence of malignancy, proved to be an abscess (1.92%) by both HPE and FNA , the details of which is shown in table 8 and figure 8 .

Table 8: DISTRIBUTION OF FOCAL LIVER LESIONS - HISTOPATHOLOGY

LESION	NUMBER OF CASES	Percentage of total %
HEPATOCELLULAR CARCINOMA	24	46.15
ADENOCARCINOMA	16	30.77
SQUAMOUS CELL CARCINOMA	1	1.92
SYNOVIAL SARCOMA	1	1.92
SECONDARIES NOT SPECIFIED	1	1.92
CHOLANGIOCARCINOMA	1	3.85
HEPATIC ADENOMA	1	1.92
HEPATOBLASTOMA	2	1.92
CARCINOMA NOT SPECIFIED	1	1.92
INADEQUATE	2	3.85
OTHERS	2	3.85
TOTAL	52	100%

Fig 8.



By FNA, 23 cases (44.23%) were diagnosed to be HCC, 15 cases (28.84%) were secondary adenocarcinomatous deposits and 2 cases (3.84%) were hepatoblastoma. Cholangiocarcinoma (1.92%), hepatic adenoma (1.92%), secondary synovial sarcoma deposit (1.92%) and secondary squamous cell carcinomatous deposit (1.92%) each contributed to one case. As with histopathology, in FNA also definitive typing of malignancy could not be done in 2 cases (3.84%) and in one case (1.92%) the smear showed evidence of secondaries liver but could not be specified. Another 4 smears (7.69%) showed no evidence of malignancy, which might be due to non representative sampling. Another case (1.92%) which had definitive radiological evidence of malignancy, proved to be an abscess by both HPE and FNA, the details of which are shown in table 9.

Table 9 : DISTRIBUTION OF FOCAL LIVER LESIONS - FNA

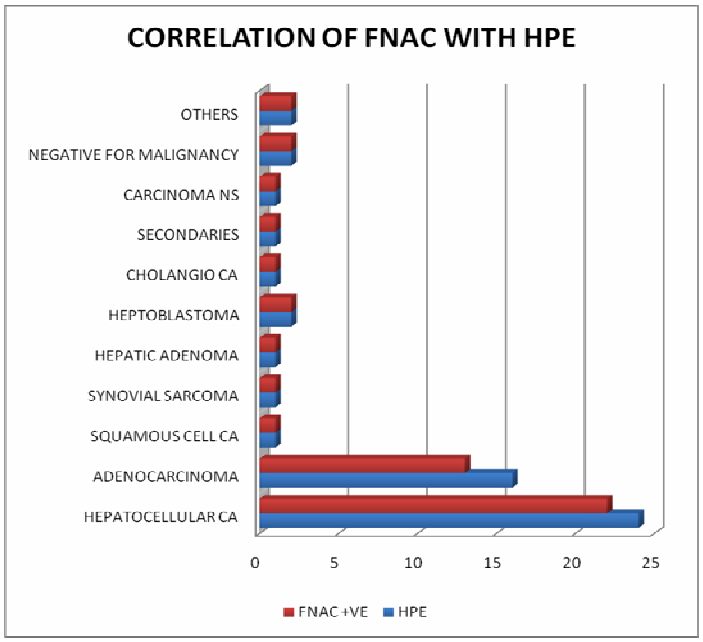
LESION	NUMBER OF CASES	PERCENTAGE OF TOTAL
HEPATOCELLULAR CARCINOMA	23	44.23%
ADENOCARCINOMA	15	28.84%
SQUAMOUS CELL CARCINOMA	1	1.92%
SYNOVIAL SARCOMA	1	1.92%
SECONDARIES NOT SPECIFIED	1	1.92%
CHOLANGIOCARCINOMA	1	1.92%
HEPATIC ADENOMA	1	1.92%
HEPATOBLASTOMA	2	3.84%
CARCINOMA NOT SPECIFIED	2	3.84%
UNREPRESENTATIVE/INADEQUATE	4	7.69%
OTHERS	1	1.92%
TOTAL	52	100%

Considering histopathology as the gold standard for definitive diagnosis of any lesion, of the 52 cases of our study, 47 cases correlated well with the FNA. Thus in 90.38% of focal liver lesions, FNA findings were consistent with that of HPE. Of the 24 cases diagnosed to be HCC by biopsy, 22 cases were also diagnosed as HCC by FNA. The percentage of correlation with respect to HCC was 91.67%. Of the 16 secondary adeno carcinomatous deposits diagnosed by biopsy, 13 cases were found to have correlated well with that of FNA (81.25%).The other cases of Cholangiocarcinoma, hepatic adenoma, hepatoblastoma, secondary synovial sarcoma deposit and secondary squamous cell carcinomatous deposit correlated well with respect to FNA and HPE. Another case which had radiological evidence of malignancy, proved to be an abscess by both HPE and FNA. For 2 cases for which definitive typing of malignancy could not be done by biopsy, FNA was also not contributory and IHC was done. Hep Par 1 was the marker used which showed positivity indicating probable origin from the hepatocytes. In 2 cases both cytology and histopathology were negative for malignancy inspite of radiological findings, which might be due to non representative sampling technique. A case of liver cell dysplasia was diagnosed by biopsy, though cytology showed evidence of adenocarcinoma which probably could be non representative sample.The results of correlation are shown in figure 9 and table 10

Table 10 : FNA – HISTOPATHOLOGY CORRELATION

LESION	HPE (n)	FNAC (n)	% of Correlation
HEPATOCELLULAR CARCINOMA	24	22	91.67
ADENOCARCINOMA	16	13	81.25
SQUAMOUS CELL CARCINOMA	1	1	100.00
SYNOVIAL SARCOMA	1	1	100.00
SECONDARIES NOT SPECIFIED	1	1	100.00
CHOLANGIOCARCINOMA	1	1	100.00
HEPATIC ADENOMA	1	1	100.00
HEPATOBLASTOMA	2	2	100.00
CARCINOMA NOT SPECIFIED	1	1	100.00
NEGATIVE	2	2	100.00
OTHERS	2	2	100.00
TOTAL	52	47	90.38

Fig 9.



Radiological diagnosis of focal liver lesions was unifocal in 22 cases (42.31%) and multifocal in 30 cases (57.69%).With respect to HCC, unifocal lesions accounted to 41.67% and multifocal 58.33% as given in table 11 and 12. The liver secondaries were unifocal lesion in 7 cases (35%) and multifocal in 13 cases (65%) as shown in table 13

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Table 11 : RADIOLOGY OF FOCAL LIVER LESIONS

UNIFOCAL	22	42.31%
MULTIFOCAL	30	57.69%
TOATL	52	100%

Fig 10

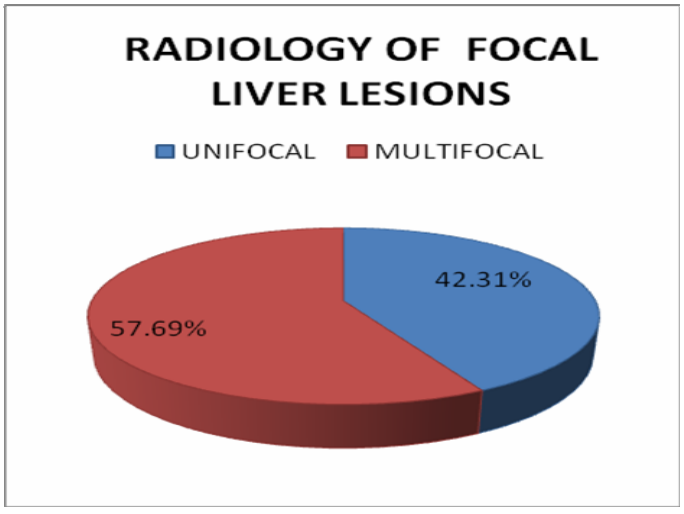


Table 12: RADIOLOGY OF HEPATO CELLULAR CARCINOMA

UNIFOCAL	10	41.67%
MULTIFOCAL	14	58.33%
TOTAL	24	100%

Fig 11

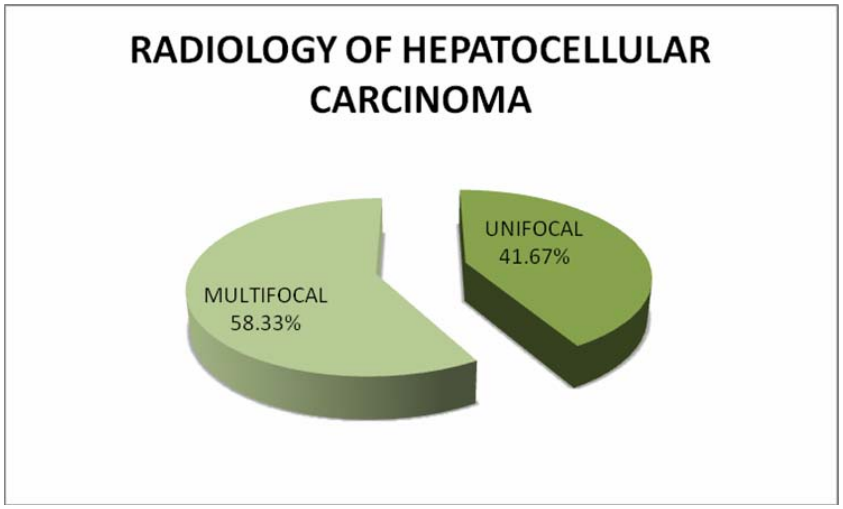
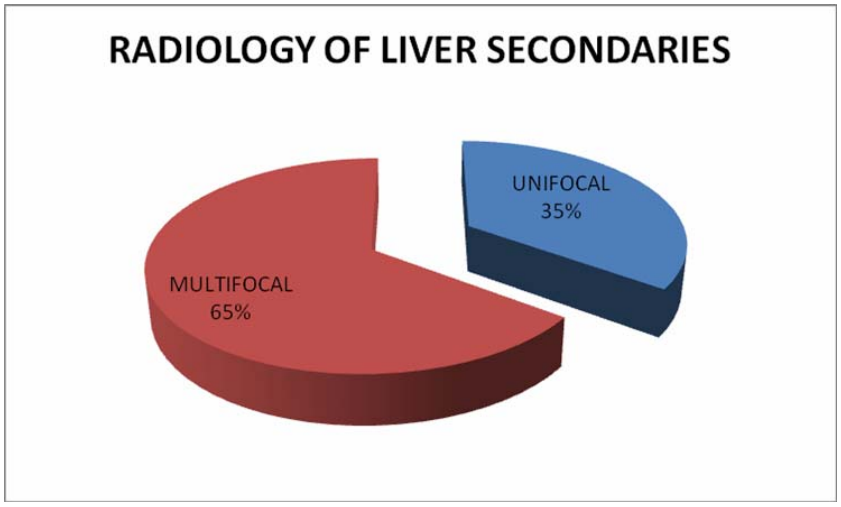


Table 13 : RADIOLOGY OF SECONDARIES

UNIFOCAL	7	35%
MULTIFOCAL	13	65%
TOTAL	20	100%

Fig 12



Radiological correlation with the histological diagnosis was 57.69 % with 30 cases of imaging diagnosis correlating well with HPE.

The liver metastases diagnosed by imaging studies (20cases) had 100% correlation with histopathology, which also diagnosed them to be secondaries of the liver. Out of 24 cases diagnosed by HPE, only 10 cases were diagnosed as HCC by US/CT imaging accounting to the correlation of 41.66% .The 2

cases diagnosed as hepatoblastoma in FNA and HPE were also diagnosed as the same in CT imaging

Table 14 : HPE & IMAGING CORRELATION IN LIVER MALIGNANCY

LESION	HPE	IMAGING	%
HEPATOCELLULAR CA	24	10	41.67
SECONDARIES	20	20	100.00
HEPATOBLASTOMA	2	2	100.00

Fig 13

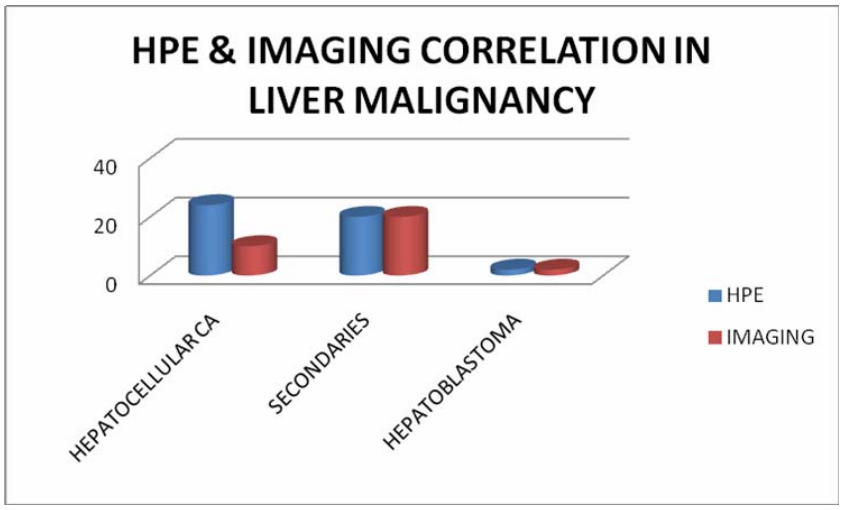


Table 15 : STATISTICAL ANALYSIS

Lesion	Sensitivity (%)	Specificity (%)	+ve predictive Value (%)	- ve predictive Value (%)	False +ve (%)	False – ve (%)
Focal liver lesion	95.7	80	97.8	66.7	20	4.3
HCC	91.66	96.42	95.65	93.5	3.57	8.34
Secondaries	85	93.75	89.5	90.9	6.25	15

The sensitivity of FNA in diagnosis of malignancy was 95.7% in our study which is in accordance with the sensitivity rates of studies by various authors like Pagani, Holm et al , Butler and Smith, Buscatine et al and Fornari et al.The specificity in diagnosing malignancy was 80%. False positive rate was 20% and false negativity was 4.3%.The low false negativity rate could be attributed to the image guidance of the procedure.The positive predictive value was 97.8% and negative predictive value was 66.7%.

FNA of HCC showed a sensitivity of 91.66% and a specificity of 96.42% of false positive rate was 3.57%, false negative rate was 8.34%, positive predictive value was 95.65% and negative predictive value was 93.10%

FNA of secondaries showed a sensitivity of 85%, specificity of 93.75%, false positive rate of 6.25%, false negative rate of 15%, positive predictive value of 89.47% and negative predictive value of 90.90% .

RESULTS OF IMMUNOHISTOCHEMISTRY

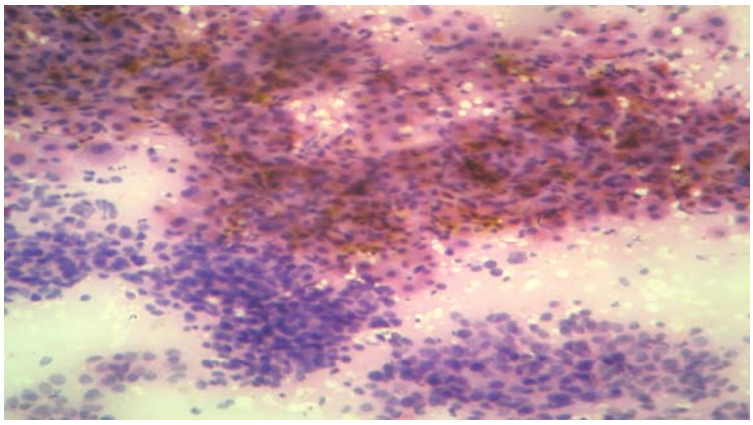
Cytokeratin was applied for almost all cases .

Hep Par 1

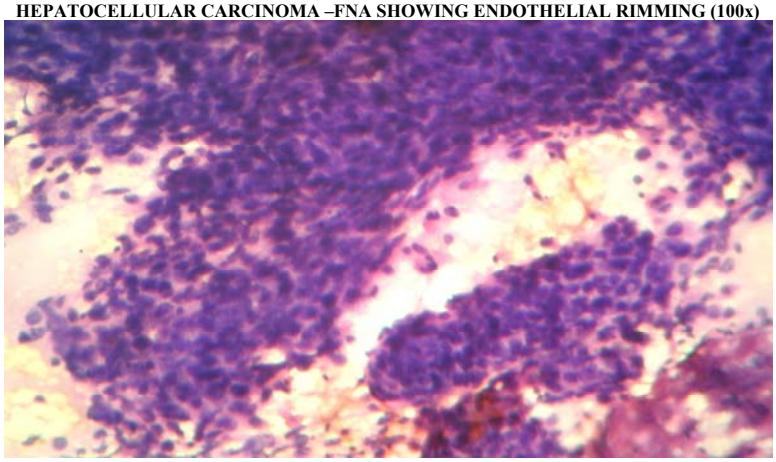
Hep Par1 was done for 10 cases. HCC was taken as a control for Hep Par1 that showed strong diffuse cytoplasmic granular positivity. The cases of hepatic adenoma and hepatoblastoma also showed strong diffuse positivity as that of HCC. Cholangiocarcinoma showed negativity for Hep Par 1, thus confirming the tissue diagnosis. The usefulness of the marker in selected cases is shown in table below;

Sl. No.	FNA Diagnosis	HPE Diagnosis	Hep Par 1	Interpretation
1.	+ve for malignancy	+ve for malignancy	-ve	-ve for HCC
2.	HCC	+ve for malignancy	++	HCC
3.	+ve for malignancy	Adenocarcinoma	+++	HCC
4.	Adenocarcinoma	HCC – Tubular Variant	+++	HCC – tubular Variant
5.	Cholangiocarcinoma	Cholangiocarcinoma	-ve	Cholangiocarcinoma

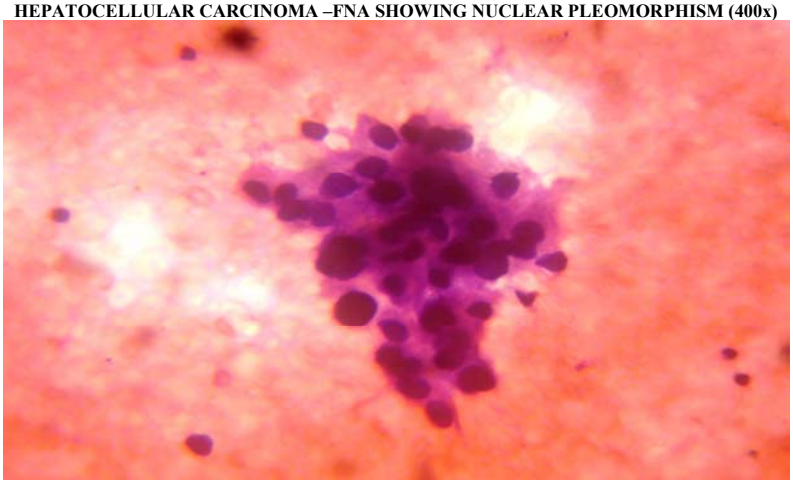
HEPATOCELLULAR CARCINOMA –FNA SHOWING BILE PLUGS (100x)



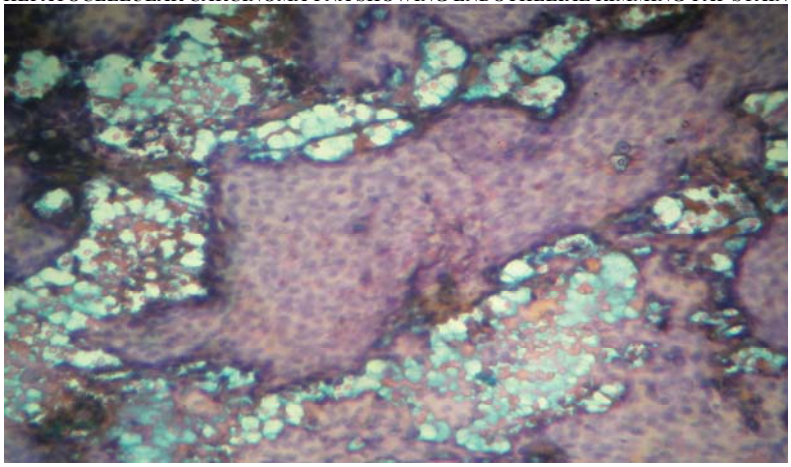
HEPATOCELLULAR CARCINOMA –FNA SHOWING ENDOTHELIAL RIMMING (100x)



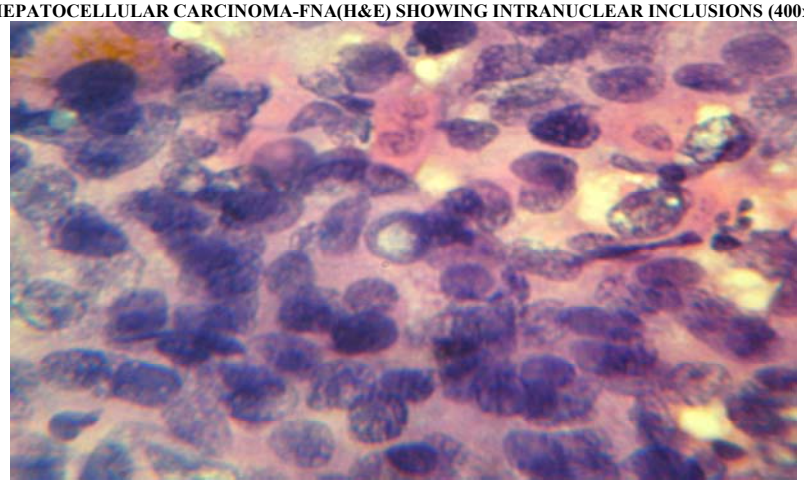
HEPATOCELLULAR CARCINOMA –FNA SHOWING NUCLEAR PLEOMORPHISM (400x)



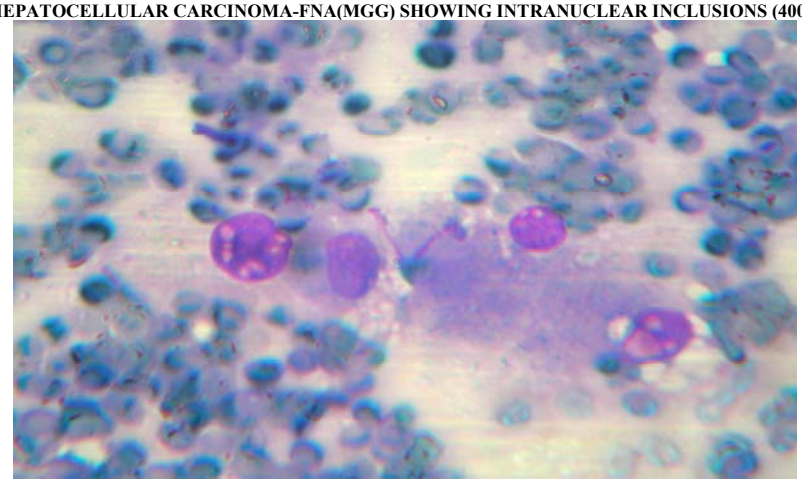
HEPATOCELLULAR CARCINOMA-FNA SHOWING ENDOTHELIAL RIMMING-PAP STAIN



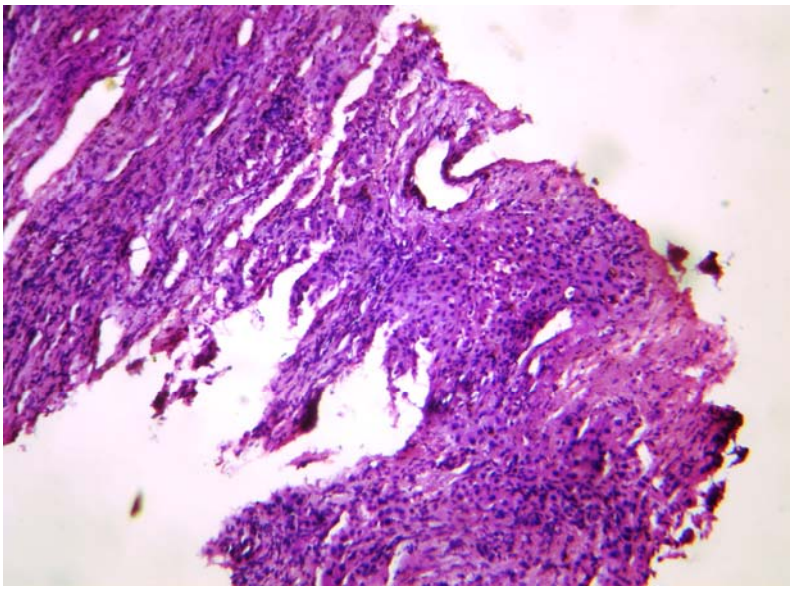
HEPATOCELLULAR CARCINOMA-FNA(H&E) SHOWING INTRANUCLEAR INCLUSIONS (400x)



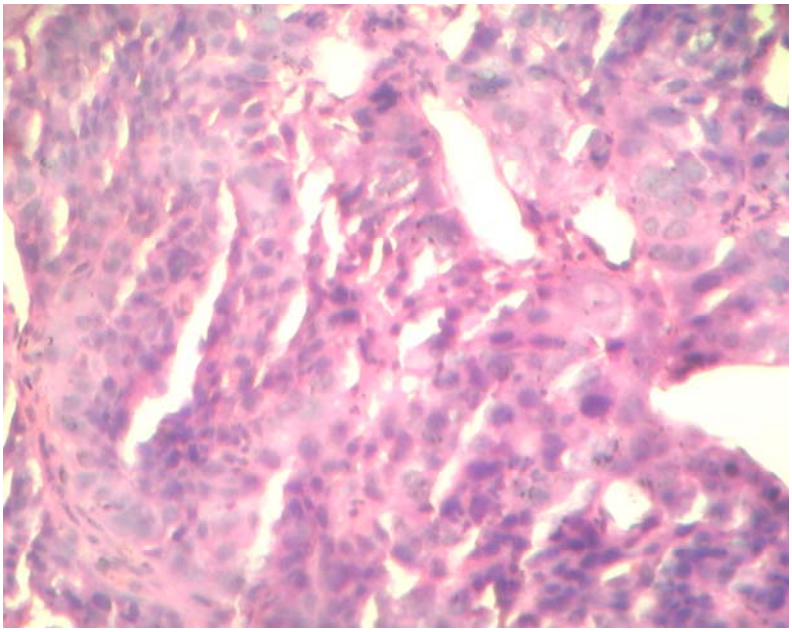
HEPATOCELLULAR CARCINOMA-FNA(MGG) SHOWING INTRANUCLEAR INCLUSIONS (400x)



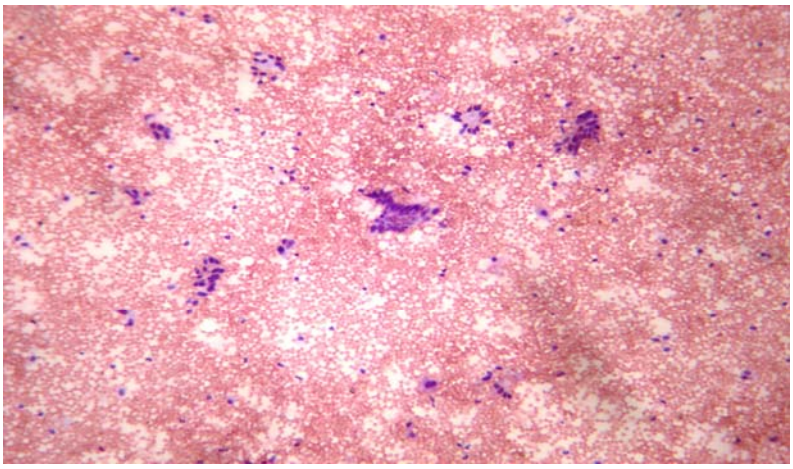
HEPATOCELLULAR CARCINOMA-HPE (100x)



HEPATOCELLULAR CARCINOMA-HPE (400x)



SECONDARY ADENOCARCINOMA-FNA (40x)



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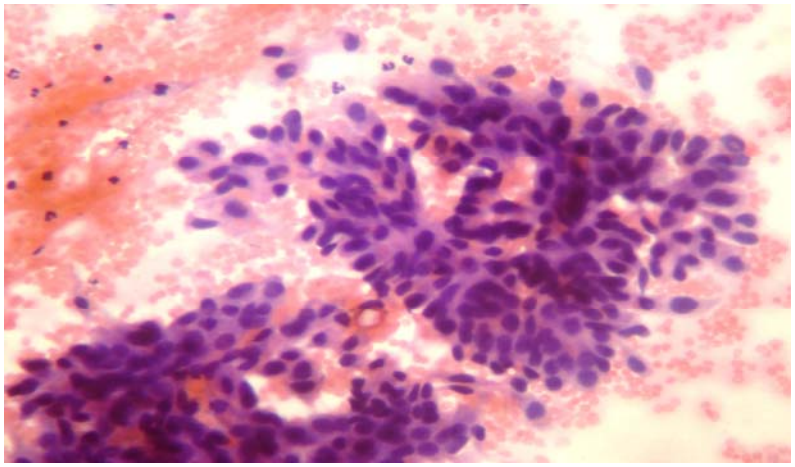

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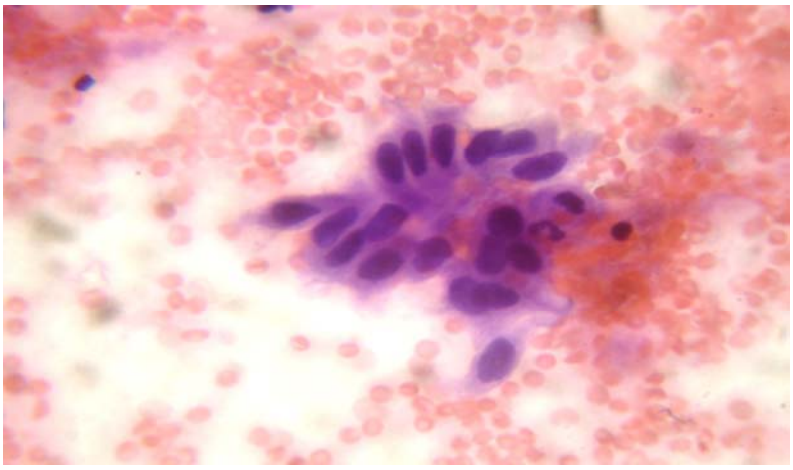

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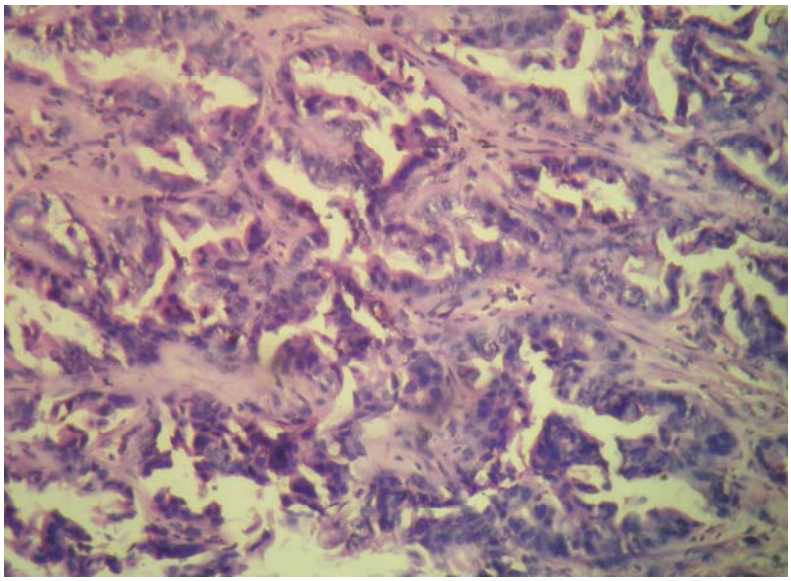

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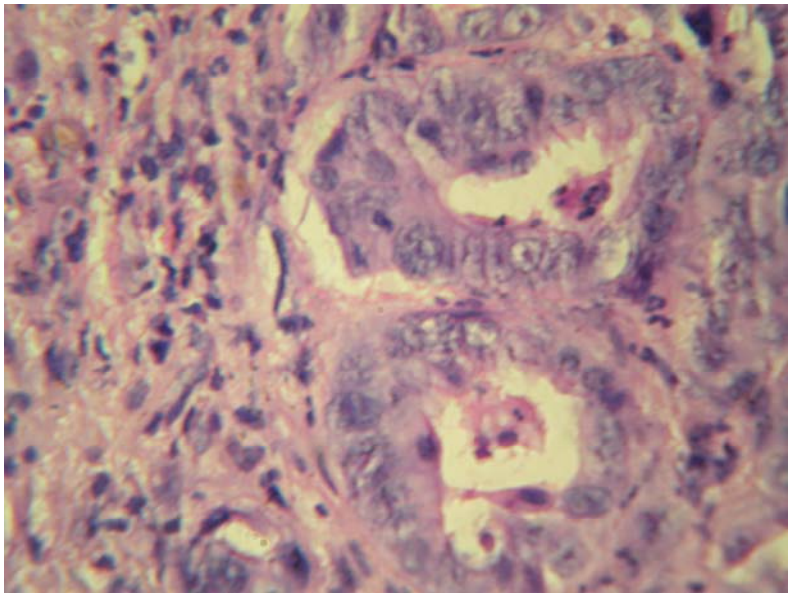
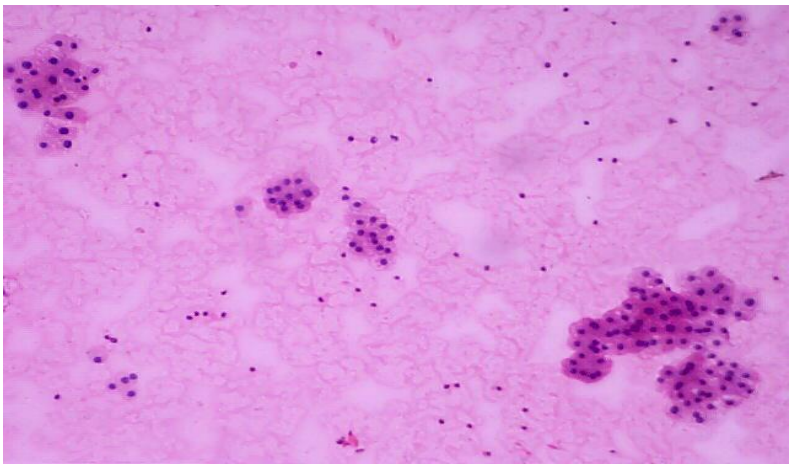
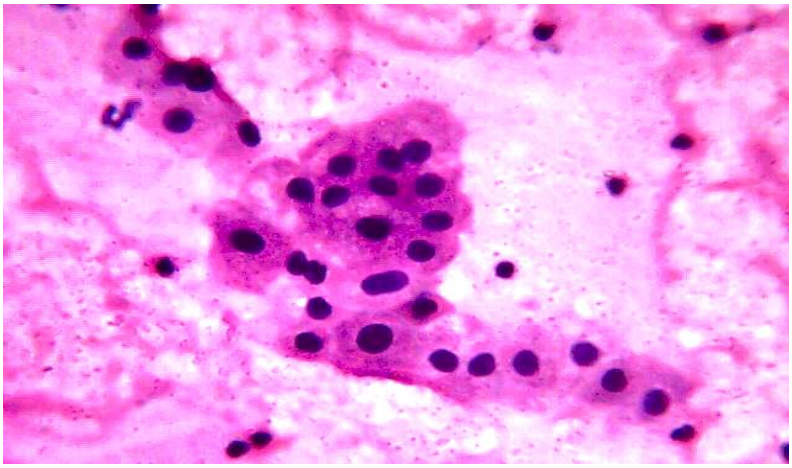


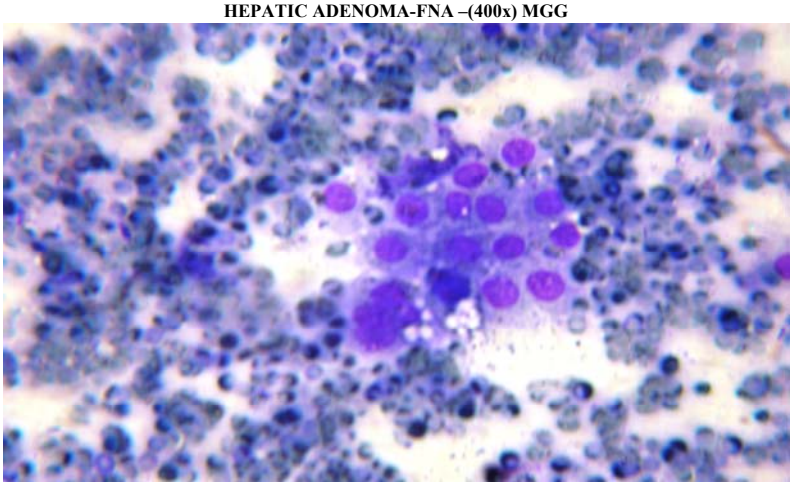
HEPATIC ADENOMA-FNA –(100x) H&E



HEPATIC ADENOMA-FNA –(400x) H&E



HEPATIC ADENOMA-FNA –(400x) MGG



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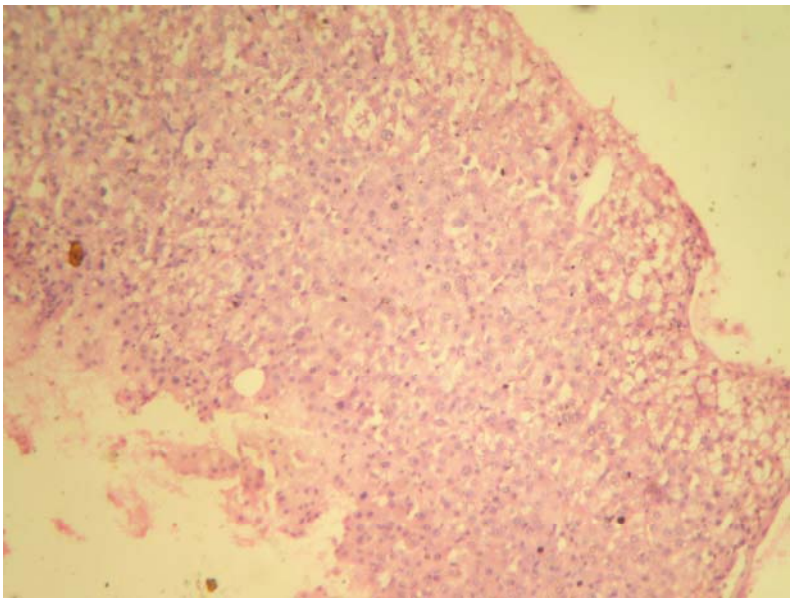

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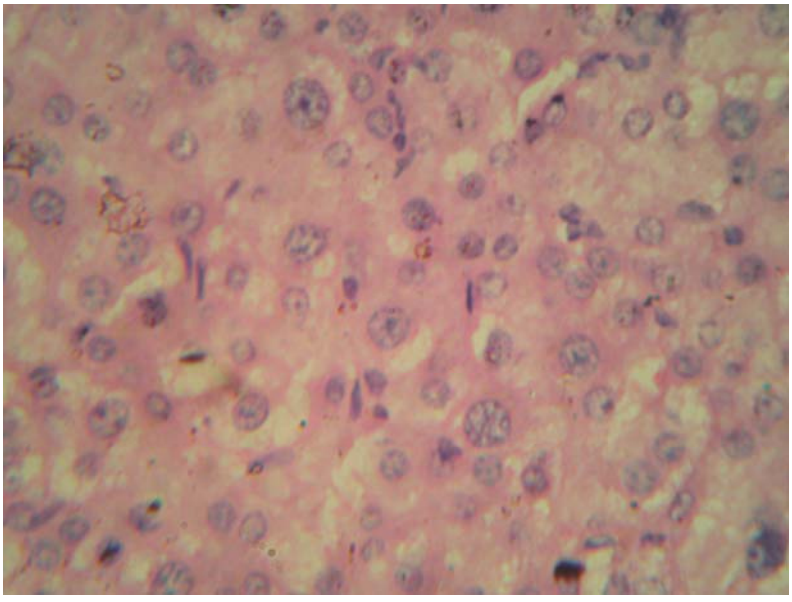
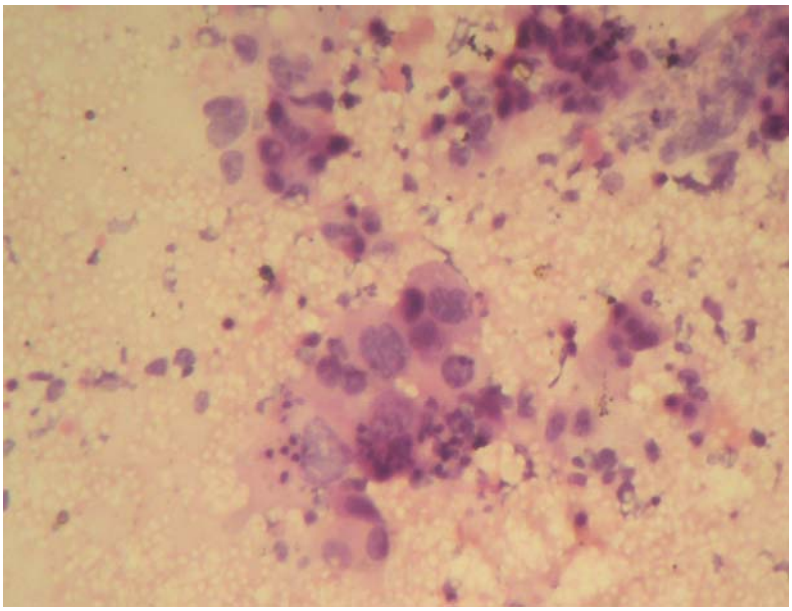
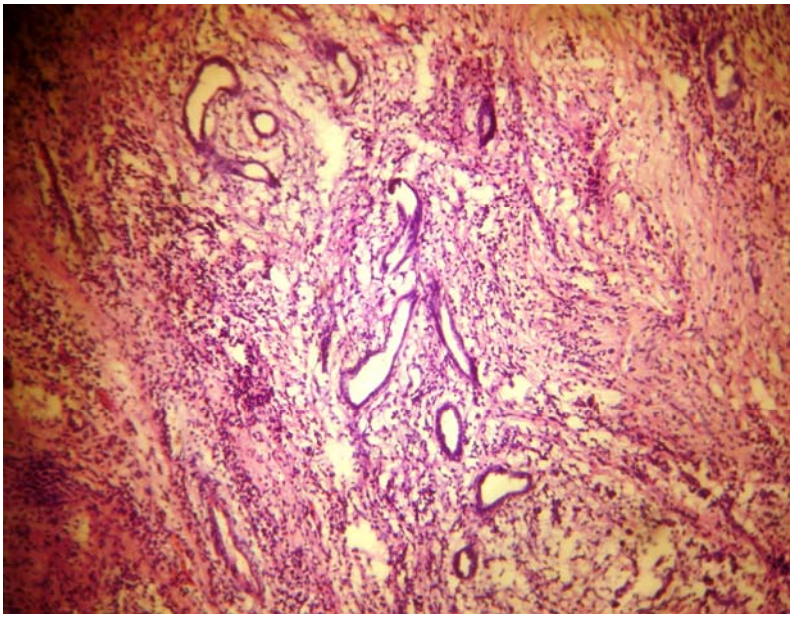


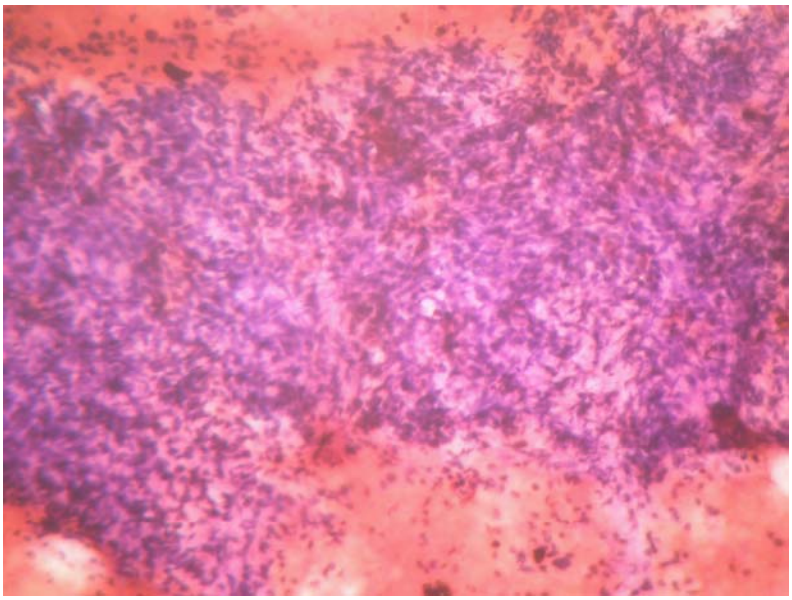
CHOLANGIOCARCINOMA-FNA (400x)



CHOLANGIOCARCINOMA-HPE (100x)



SECONDARY SYNOVIAL SARCOMA DEPOSIT-FNA (100x)



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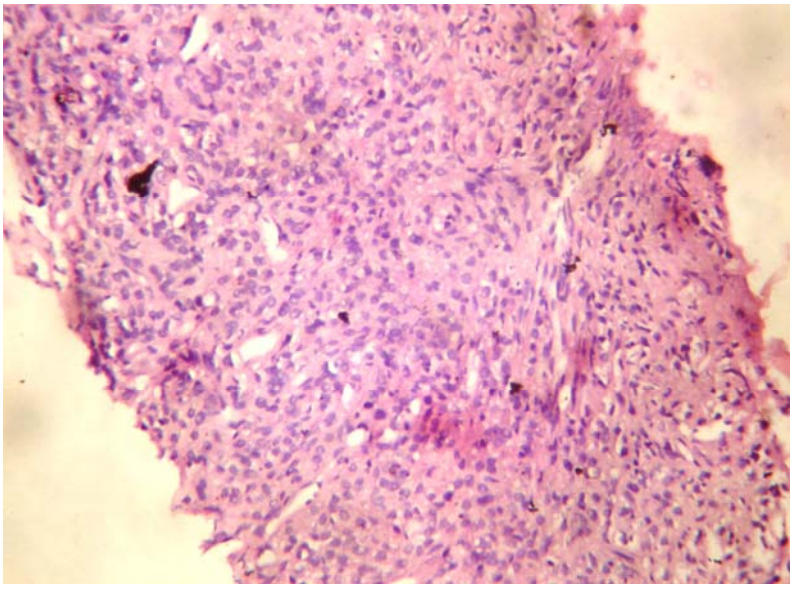
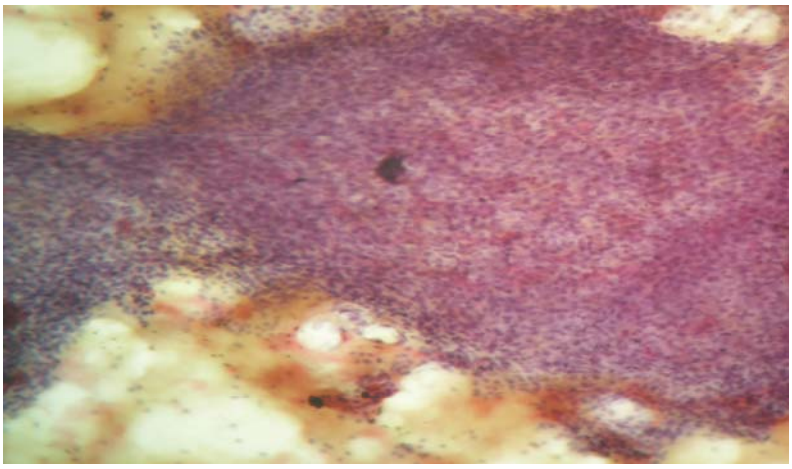
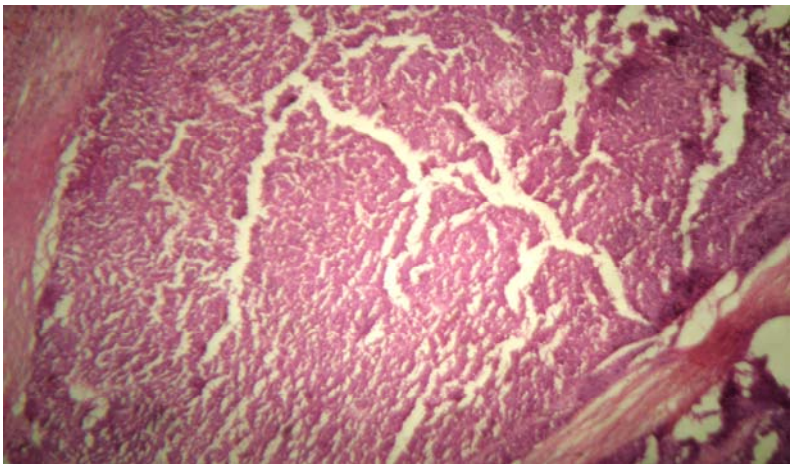


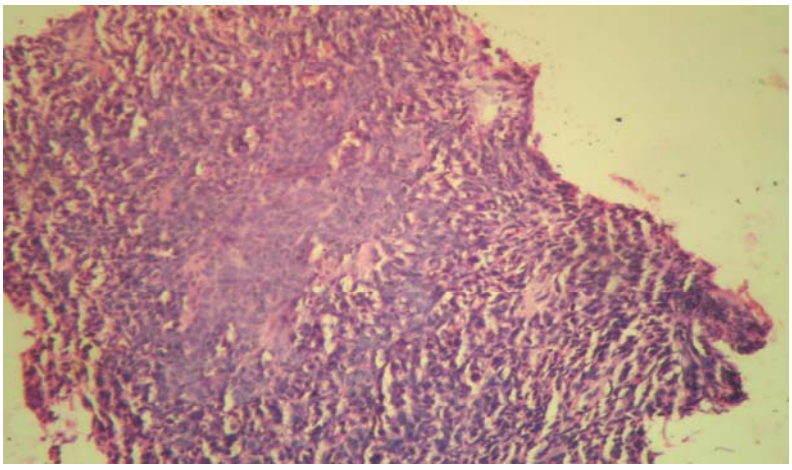
HEPATOBLASTOMA-FNA (100x)



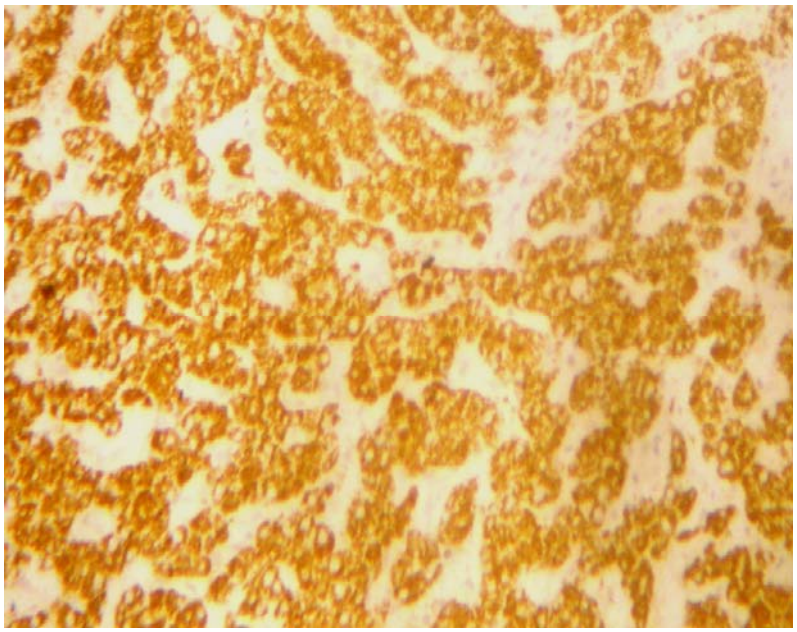
HEPATOBLASTOMA-HPE (100x)



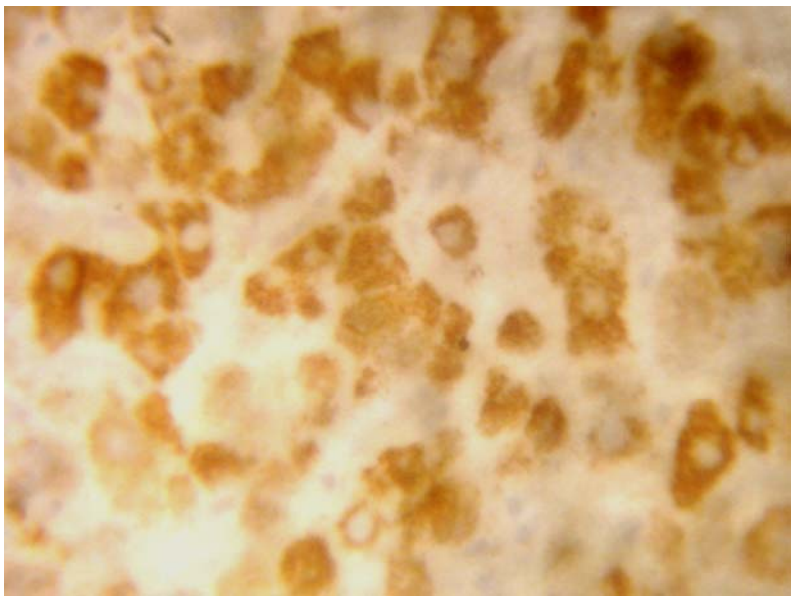
SECONDARY SQUAMOUS CELL CARCINOMATOUS DEPOSIT-HPE (100x)



IMMUNOHISTOCHEMISTRY-Hep Par 1 (100x)

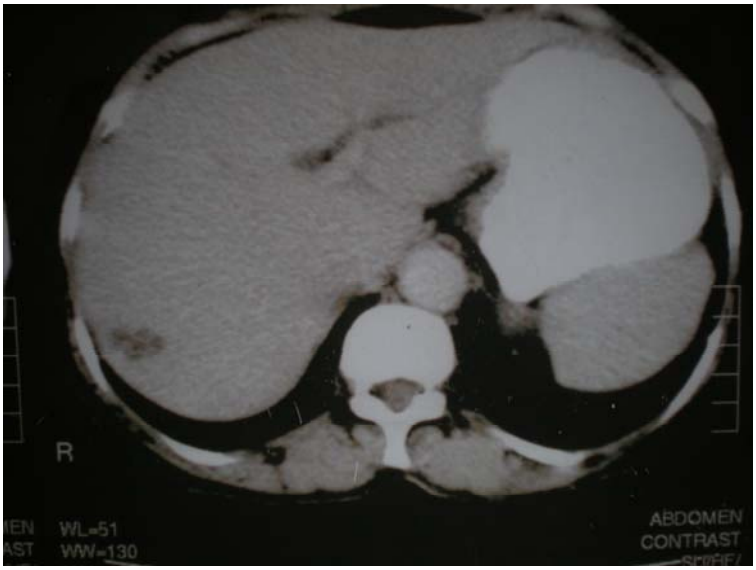


IMMUNOHISTOCHEMISTRY-Hep Par 1 (400x)



HEPATOCELLULAR CARCINOMA

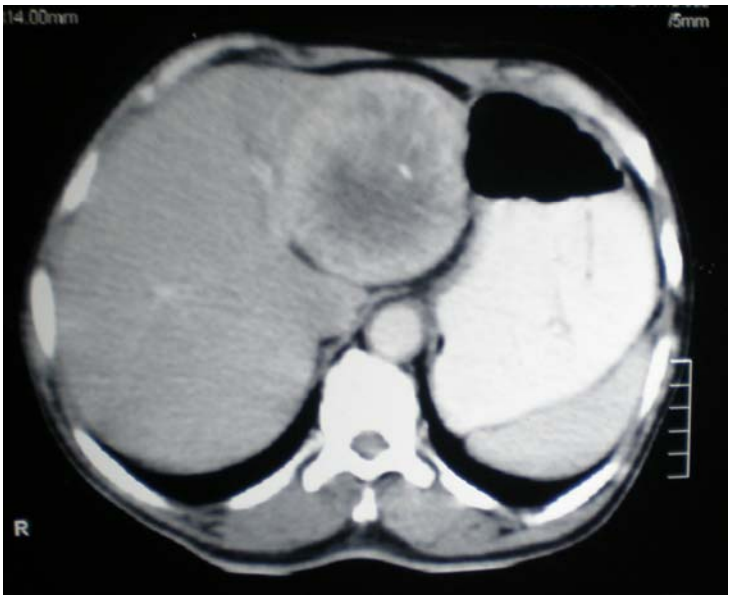
UNIFOCAL LESION - CECT



MULTIFOCAL LESION - CECT

SECONDARIES LIVER

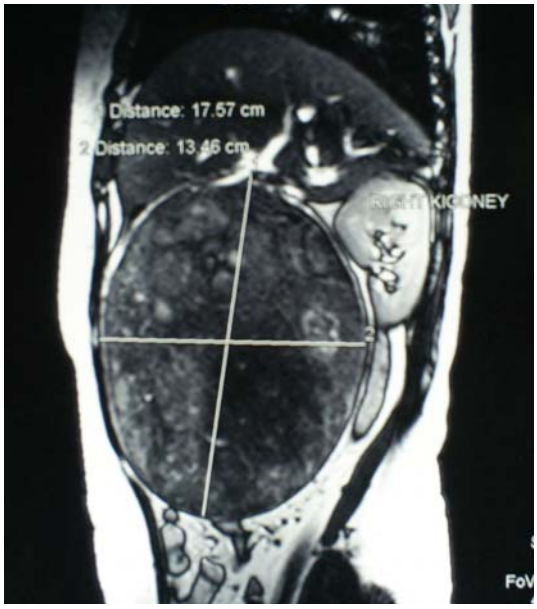
UNIFOCAL LESION - CECT



MULTIFOCAL LESION - CECT

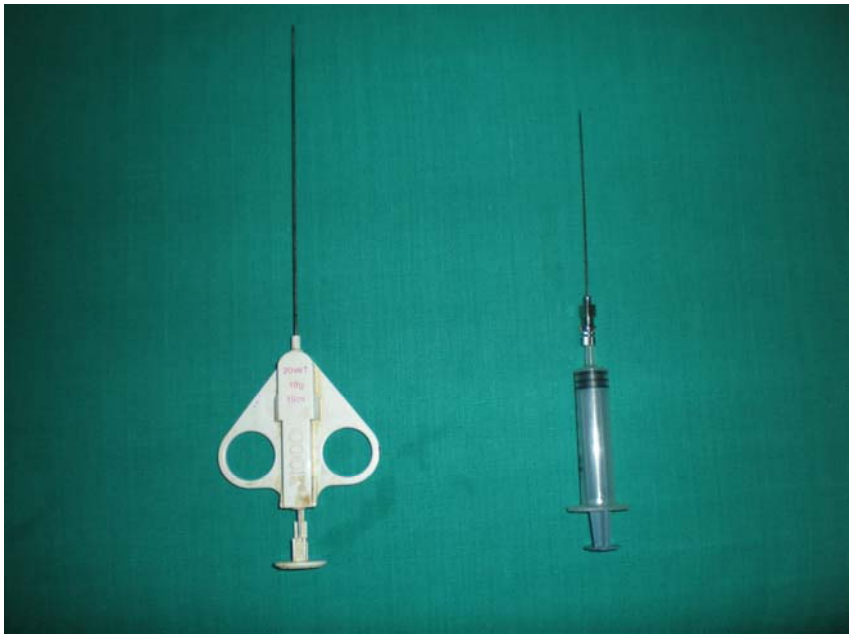
HEPATIC ADENOMA

SPIRAL CT – SAGITTAL SECTION



SPIRAL CT CORONAL SECTION

TRUCUT BIOPSY GUN (18G) AND FINE NEEDLE ASPIRATION SYRINGE WITH NEEDLE (20G)



DISCUSSION

Literature supports the usefulness of FNA in diagnosing benign and malignant liver lesions. The overall sensitivity varies from 67-100% in diagnosing malignant liver lesions. The specificity was 99%. The positive predictive value was 99%, whereas the negative predictive value was 71%. This was in accordance to our study with sensitivity of 95.7%, specificity of 80%, positive predictive value of 97.8% and the negative predictive value of 66.7%. The experiences of some of the authors are given below:

Table 16 : COMPARISON WITH STANDARD STUDIES

Author	No of patients	Type of lesion	Sensitivity (%)	Specificity	PVpos	PVneg
Montali et al 1982	108	M	92	100	100	70
Rosenblatt et al 1982	59	M	94	100	100	80
Whitlach et al 1984	86	M	87	100	100	76
Tatsuta et al 1984	41	M	94	96	94	96
Gabel et al 1986	854	M	88	100	-	-
Servol et al 1988	175	M	80	100	100	76
Buscatine et al 1990	972	M	91	99	100	77
Fornari et al 1990	441	M	93	100	100	84

Author	No of patients	Type of lesion	Sensitivity (%)	Specificity	PVpos	PVneg
Jacobson et al 1983	55	S	100	100	100	100
Pagani 1983	100	S	95	100	100	56
Schwerk et al 1983	130	S	92	93	98	77
Droese et al 1984	100	S	94	100	100	89
Haubek 1985	380	S	91	100	100	65
Holm et al 1985	247	S	92	100	100	60
Bell et al 1986	197	S	67	100	100	45
Butler & smith 1989	40	S	98	100	100	88
Edoute et al 1991	321	S	86	98	99	76
Ohlsson et al 1999	178	S	89	67	98	27
Our study	52	S	95.7	80	97.8	66.7

S; solid liver lesions: M ;liver masses of any type

The relationship between size of lesion and proportion in which a correct diagnosis was made was studied by Reading et al (1988)[40] and correct diagnosis was made by FNA in 79% of lesions 1 cm or less in diameter . False positive were due to sampling error or are were based on aspiration material that often was scanty.With regard to HCC, FNA is accurate with a sensitivity rate 80 to 95% and a specificity of 100%.[41,42,43]

Jacobsen et al 1983 , Droese et al 1984 , Hajdu et al 1989, Fornari et al 1990, Edoute et al 1991 were able to produce the cytological diagnosis which corresponds closely to histology of the tumor.

There is no agreement as to the superiority of cytology or microhistology in the diagnosis of focal liver lesions

Table 17

Author	No of patients	Sensitivity Cytology %	Sensitivity Histology %
Wittenberg et al 1982[44]	65	81	73
Sangalli et al 1989[45]	112	74	82
Buscarini et al 1990[46]	969	91	94
Edoute et al 1991[47]	34	32	62
Rapaccini et al 1994[48]	73	80	61
Nyman et al 1995[49]	69	62	91

Fang-Ying Kuo et al 2004[50]	936	78.4	76.3

From the comparative studies shown above, it is evident that neither method has clear advantages and the retrieval rates and tissue typing accuracies are fairly similar.

The cytology may be inadequate in some patients , particularly in those with vascular lesions, in fibrotic, dense tumors, in lymphomas and in well differentiated primary liver cancer.

Edoute et al[51] in 1991-1996 prospectively studied the accuracy of non guided FNA of liver lesions in 107 patients. The sensitivity was 81%, specificity 100%, positive predictive value 100%, negative predictive value 85%.The overall diagnostic accuracy rate was 91%. The relationship between non guided FNA (true +ve &false –ve) and type of suspected malignant liver lesions demonstrated by different kinds of imaging (Radioisotope, ultrasound, CT among 52 patients with malignant liver disease was also studied by them.

Table 18 : COMPARISON OF IMAGING FINDINGS WITH STANDARD STUDIES

AUTHOR	UNIFOCAL	MULTIFOCAL
Edoute et al	26%	74%
Our study	42%	58%

Accuracy of various imaging modalities in diagnosing HCC according to Colli et al[52] in 2006 is given below:

Table 19 : COMPARISON OF IMAGING FINDINGS WITH STANDARD STUDIES

Imaging technique	No of studies	Sensitivity	Specificity
US	14	60	97
CT	10	68	93
MRI	9	81	85

In our study the sensitivity of CT was 68% and specificity was 80%.

Bakshi et al[53] in 2006 correlated 41 FNA from pediatric liver SOL with clinical, radiological findings and histopathological diagnosis. The overall FNA sensitivity was 95%, specificity was 100%, positive predictive value was 100% and negative predictive value was 92.3% and diagnostic accuracy was 96.9%.In our study, the 2 cases of pediatric liver SOL reported as hepatoblastoma in FNA, correlated well with the imaging and histopathological diagnosis.

CJR Stewart et al[54] compared the sensitivity and specificity of percutaneous FNA and needle core biopsy in the diagnosis of suspected abdominal malignancies and observed that combination of these two techniques, the sensitivity was 90.7% and the specificity was 100% for both

methods and proved that sensitivity increased with image guidance than direct aspiration.They proved FNA was 2-24% more sensitive than needle core biopsy.

Yu and Coworkers (1998)[55] have studied diagnostic efficacy of FNA using an 18 gauge automated cutting needle in small (3cm or less) focal hepatic lesions of different pathologies and different sizes (≤1cm; 1-2cm; 2-3cm).The sensitivity for diagnosing malignancy was 96%, specificity 100%, positive and negative predictive value were 100 and 96% respectively.

In 1983 Jacobson et al[56] compared the coarse needle biopsy versus fine needle aspiration biopsy in the diagnosis of focal liver lesions of 55 patients. Our study also showed the same results as given below:

Table 20 : COMPARISON WITH STANDARD STUDY

Author	No of patients	Core needle biopsy	FNAB
Jacobson et al 1983	55	41malignant 7-ve 7-ve	41 malignant 7-ve 7+ve
Our study	52	46 malignant 4-ve 2-ve	46 malignant 4-ve 2+ve

FNA is an effective and safe method for the diagnosis of focal hepatic lesions, with diagnostic accuracy similar to that of CNB. When the 2

techniques are combined, the accuracy of the diagnosis of malignancy of focal liver lesion increases.[57]

Xu GA in 1989[58] compared the accuracy rate of ultrasound, FNA and HPE and the results were found to be higher for FNA (95.2%) than US (86.7%).This was in concordance with accuracy rate of our study(94.23%).

Isin Soyuer et al[59] in 2003 analysed 17 cytologic and 5 architectural features in a series of 320 FNAs from HCC and compared them with 73 FNAs with benign lesions and with 705 FNAs from metastatic carcinoma. The sensitivity of FNA for hepatic malignancy was 99.5% and specificity was 100%. Bile, centrally placed nuclei and intranuclear inclusions were the most specific cytologic criteria of HCC with trabecular pattern consisting of sinusoidal capillarization and endothelial rimming of the malignant hepatocytes as the predominant pattern. In our study also the smears of HCC showed similar characteristic features.

Devi VL et al[60] also found that trabecular pattern covered by endothelium was the most common pattern in a study of smears of 32 cases of FNA of HCC as in our study.

CONCLUSION

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The following are the conclusions arrived by this study

- Primary hepatocellular carcinoma is the most common malignancy in our study (46.15%), followed by metastatic adenocarcinomatous deposits (30.77%).

- Males formed the majority of the cases of focal liver lesions, with peak incidence between 61-70 yrs.

- HPE and imaging correlation is 57.69%.

- Taking HPE as the gold standard for correct diagnosis, the correlation of FNA with HPE diagnosis is 90.68%.

- With respect to HCC, the correlation of FNA with HPE is 91.67%.

- Correlation of secondary adenocarcinomatous deposits is 81.25% .

- The results of image guided FNA in our study:

  Sensitivity is 95.67%

  Specificity is 80 %

  False positive rate is 20%

  False negative rate is 4.25%

Positive predictive value is 97.8%

Negative predictive value is 66.7%

- With application of above parameters the diagnostic accuracy of FNA is 94.23%

- There were no major complications encountered.

- US guidance increases the accuracy of diagnosing the malignancies of the liver.

- FNA is useful in the diagnosis of focal liver lesions and trucut biopsy is helpful in tumor typing , grading and determination of primary site of origin in metastatic lesions.

- The combination of FNA and trucut biopsy should be considered complementary diagnostic techniques.

- Immunohistochemistry is helpful in doubtful cases to prove tumour origin.

- The accuracy of diagnosis in FNA and HPE is almost similar indicating that the simple and safe technique of US guided FNA is a little superior to HPE and in correlation with serum markers could be an effective alternative method for biopsy.

- From this study it has been proved that FNA technique yielded higher number of positive diagnosis of malignancy than obtained with core needle, because aspirated material obtained with fine needle, represents a considerably larger area since repeated aspirations are performed in various directions.

Ultrasound guided FNA of liver lesions is a rapid, inexpensive, safe, highly accurate and minimally invasive technique for obtaining a tissue diagnosis in solid focal lesions of the liver.

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MASTER CHART

S.NO	FNAC NO	HPE NO	SEX	AGE	JAUNDICE	HEPATOMEGALY	PHT	LIVER FAILURE	LOA/LOW	ABNORMAL C0AGULATION	↑SR. BILIRUBIN	↑SAP	HBS Ag	AFP	SGOT/SGPT	U/S	CT SCAN	UNIFOCAL	MULTIFOCAL	IMAGING DIAGNOSIS	FNA DIAGNOSIS	HPE DIAGNOSIS
1	2535/07	6820/07	M	65	-	√	-	-	√	-	-	↑	-	-	-	√	-	√	-	SEC	+VE	ACA
2	3778/07	7611/07	M	64	-	√			√					-	-	√	-	-	√	HCC/SEC	HCC	HCC
3	5263/07	7596/07	M	35	√	√	√	-	√	-	-	-	-	-	↑	√	√	√	-	HCC	HCC	HCC
4	5321/07	7697/07	M	65	-	√	-	-	-	-	-	-	-	-	-	√	√	-	√	SEC	HCC	HCC
5	5529/07	8021/07	M	60	-	√	-	-	√	-	-	√	-	-	↑	√	√	√	-	HCC	HCC	HCC
6	5651/07	8261/07	M	72	-	-	-	-	√	-	-	-	-	↑	-	√	√	√	-	HCC	+VE	+VE
7	5827/07	8582/07	F	21	-	√	√	-	√	-	-	-	-	-	-	√	√	√	-	MASS	HCA	HCA
8	1125/07	4347/07	F	48	√	√	-	-	√	-	↑	-	-	-	-	-	√	-	√	SEC	ACA	ACA
9	5833/07	8604/07	M	67	-	√	-	-	-	-	-	-	-	-	-	√	√	√	-	AB	HCC	HCC
10	5870/07	8848/07	M	67	-	-	-	-	-	-	-	-	-	-	-	√	-	√	-	AB	AB	AB
11	5998/07	8897/07	M	37	√	√	-	-	-	-	-	-	-	-	-	√	√	√	-	HCC	HCC	HCC
12	6019/07	2933/07	M	68	-	√	√		√	-	-	-	-	-	-	√	√	-	√	HCC	HCC	HCC
13	112/08	162/08	M	75	-	√	√	-	√	-	-	-	-	-	-	√	√	√	-	HCC	HCC	HCC
14	117/08	144/08	M	56	√	√	√	-	-	-	-	-	-	-	-	√	√	-	√	HCC	HCC	HCC
15	922//O7	3441/07	M	60	-	√	-	-	√	-	-	-	+VE	-	-	-	√	√	-	HCC	HCC	HCC
16	414/08	697/08	F	35	-	-	-	-	-	-	-	-	-	-	-	√	√	-	√	SEC	ACA	ACA
17	415/08	698/08	M	32	√	√	√	√	√	-	↑	↑		-	-	-	√	-	√	HCC	HCC	ACA
18	875/08	1318/08	F	42	-	√	√	-	√	-	-	↑	-	-	-	√	√	-	√	SEC	ACA	ACA
19	1012/08	1547/08	F	60	-	-	-	-	√	-	↑	↑	-	-	-	√	-	-	√	SEC	-VE	-VE
20	1007/08	1553/08	M	70	-	√	-	-	√	-	↑	-	-	-	-	√	√	-	√	SEC	A CA	ACA
21	1047/08	1597/08	F	40	-	√	-	-	√	-	-	-	-	-	-	-	√	√	-	SEC	HCC	HCC
22	5770/08	8521/08	M	47	√	√	-	-	√	-	↑	-	-	-	-	-	√	-	√	HCC	HCC	HCC
23	1224/08	1813/08	F	63	-	√	-	-	√	-	-	-	-	-	-	√	√	-	√	SEC	-VE	-VE

24	1250/08	1852/08	M	40	-	√	√	-	√	-	-	↑	-	↑	↑	-	√	-	√	SEC	ACA	ACA
25	1406/08	2077/08	M	60	-	√	√	√	√	-	↑	↑	-	-	↑	√	√	√	-	SEC	ACA	ACA
26	1376/08	2932/08	M	55	√	√	-	-	√	-	↑	-	-	-	↑	√	√	-	√	SEC	HCC	HCC
27	1398/08	2144/08	M	55	-	√	√	√	√	-	↑	↑	-	-	↑	√	-	-	√	HCC	HCC	HCC
28	1532/08	2264/08	F	38	-	√	-	-	√	-	-	↑	-	-	-	√	√	√	-	SEC	ACA	ACA
29	336/07	96/07	M	6	-	√	-	-	-	-	-	-	-	↑	-	-	√	√	-	HBL	HBl	HBL
30	39/07	147/07	F	10	-	√	-	-	-	-	-	-	-	-	-	-	√	√	-	HBL	HBL	HBL
31	1813/08	2702/07	M	70	-	-	-	-	-	-	-	↑	-	-	↑	√	√		√	HCC	HCC	HCC
32	2266/08	3255/08	M	52	√	√	√	-	√	-	-	-	-	-	↑	√	√	√		HCC	HCC	HCC
33	2346/08	3356/08	M	65	√	√	-	-	√	-	↑	-	-	-	-	√	√	-	√	SEC	2*CA	2*CA
34	2450/08	3440/08	M	70	-	√	-	-	√	-	-	-	-	-	-	√	√	√	-	SEC	2*SS	2*SS
35	2504/08	3487/08	F	65	-	√	-	-	√	-	-	-	-	-	-	-	√	-	√	SEC	ACA	ACA
36	2540/08	3511/08	F	41	-	√	-	-	√	-	-	-	-	-	-	√	√	-	√	SEC	HCC	HCC
37	2503/08	3517/08	M	60	√	√	√	√	√	-	↑	-	+VE	-	↑	√	√	-	√	HCC	HCC	HCC
38	2980/08	4065/08	M	62	-	√	-	-	-	-	-	-	-	-	-	√	√	√	-	HCC	ACA	ACA
39	3109/08	4280/08	M	69	-	√	-	-	-	-	-	↑	+VE	-	-	√	√	-	√	SEC	ACA	ACA
40	3222/08	4409/08	M	40	√	√	-	-	√	-	↑	↑	-	-	-	√	-	-	√	HCC	ACA	ACA
41	3258/08	4435/08	M	68	-	√	-	-	-	-	-	-	-	-	-	-	√	-	√	HCC	ACA	LCD
42	3272/08	4455/08	M	45	-	√	-	-	√	-	-	↑	-	↑	↑	√	√	-	√	HCC/SEC	ACA	HCC
43	3366/08	4527/08	F	37	-	-	-	-	-	-	-	↑	-	-	↑	-	√	√	-	HCA/FNH	HCC	HCC
44	3645/O8	4957/08	F	50	-	-	√	-	√	-	--	-	-	-	-	√	√	-	√	SEC	HCC	HCC
45	3574/08	4875/08	F	45	√	√	-	-	-	-	-	-	-	-	-	-	√	√	-	CCA	CCA	CCA
46	3536/08	5101/08	M	55	√	√	-	√	√	-	↑	↑	-	-	↑	-	√	-	√	HCC	HCC	HCC
47	1850/08	5345/08	M	55	√	√	-	-	-	-	-	-	-	-	-	-	√	-	√	SEC	SCC	SCC
48	4205/08	5770/08	M	55	√	√	√	√	√	-	↑	-	-	-	-	√	√	-	√	SEC	HCC	HCC
49	2634/07	7205/07	M	68	√	√	-	-	√	-	↑	↑	-	↑	↑	-	√	√	-	HCC	-VE	HCC
50	2712/07	7286/O7	M	50	√	√	√	√	√	-	↑	↑	-	-	↑	-	√	-	√	SEC	-VE	ACA
51	3108/08	4214/08	M	64	-	√	√	√	√	-	↑	↑	-	-	↑	√	√	√		SEC	ACA	ACA
52	5254/08	7068/08	M	67	-	√	-	-	√	-	↑	-	-	-	-	-	√	-	√	HCC	ACA	ACA

KEY TO MASTER CHART

HCC	-	Hepatocellular Carcinoma
ACA	-	Adenocarcinoma
HCA	-	Hepatic Adenoma
HBL	-	Hepatoblastoma
SS	-	Synovial Sarcoma
SCC	-	Squamous Cell Carcinoma
SEC	-	Secondaries
CaNS	-	Carcinoma Not Specified
AB	-	Abscess
LCD	-	Liver Cell Dysplasia
CA	-	Carcinoma
FNA	-	Fine Needle Aspiration
HPE	-	Histopathological Examination
LOA	-	Loss of Appetite
LOW	-	Loss of Weight
PHT	-	Portal Hypertension
SAP	-	Serum Alkaline Phosphatase
SGOT	-	Serum Glutamate Oxaloacetate Transaminase
SGPT	-	Serum Glutamate Pyruvate Transaminase
HBsAg	-	Hepatitis B Surface Antigen
AFP	-	Alfa Fetoprotein
US	-	Ultra Sound
CT	-	Computerised Tomography

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INSTITUTIONAL ETHICAL COMMITTEE
GOVERNMENT GENERAL HOSPITAL & MADRAS MEDICAL COLLEGE,
CHENNAI-600 003.

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K.Dis.No.16328 P & D3/Ethies/Dean/GGH/08 Dated: 8/9/2008

Title of the work : "Radiological and Histological correlation of USG guided FNAC of Focal Liver lesions."

Principal Investigator : Dr. Chitralega Sugumar

Department : Pathology, MMC & GGH Ch.3.

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 10th sep 2008 at 2 P.M in GGH Deans, Chamber, Chennai-3.

The members of the Committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The principal investigator and their term are directed to adhere the guidelines given below:

1. You should get detailed informed consent from the patients/participants and maintain confidentiality.
2. You should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution / Government.
3. You should inform the IEC in case of any change of study procedure, site and investigation or guide.
4. You should not deviate form the area of the work for which I applied for ethical clearance.
5. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
6. You should abide to the rules and regulations of the institution(s)
7. You should complete the work within the specific period and if any extension of time is required, you should apply for permission again and do the work.
8. You should submit the summary of the work to the ethical committee on completion of the work.
9. You should not claim funds from the Institution while doing the work or on completion.
10. You should understand that the members of IEC have the right to monitor the work with prior intimation.

SECRETARY
IEC, GGH,CHENNAI

CHAIRMAN
IEC, GGH, CHENNAI

DEAN
GGH &MMC, CHENNAI

RKM.5.6(2)

PROFORMA

Name: Age: Sex: IP No:

Address: Ref unit:

History:

1	Smoker	
2	Alcoholic	
3	Drugs	
4	DM/HT/TB	
5	Family H/O	

Symptoms:

1. Pain
2. Fever
3. Jaundice
4. Loss of weight/loss of appetite
5. S/S of portal hypertension
6. S/S of liver failure
7. Palpable mass
8. Asymptomatic

General Examination:

1. Anemia
2. Jaundice
3. Lymphadenopathy
4. Ascites
5. Portal hypertension

Local Examination:

1. Hepatomegaly
2. Other masses

Investigation:

1. Complete Hemogram
2. Coagulation profile
3. LFT
4. Urine
5. Viral markers
6. Serum AFP
7. USG:

8. CT:

9. FNAC:

10. Trucut biopsy:

Diagnosis:

Complication:

Treatment: